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Editorial

Geriatric Healthcare in Pakistan

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Editor

Pakistan is beset with a paradox when it comes to care of the elderly, a discipline termed 'geriatrics' in medicine. On the one hand, there is absence of care-giving institutional support in the public system, while on the other, there is a strong culture of family support, with members of the immediate family inevitably serving as care-givers for the elderly.

It may take a few years before support for the elderly in Pakistan declines to the extent seen in the west, where families tend to be much more atomized and scattered. They are hence more unlikely, unwilling, or unable to care for old and ailing parents in the comfort of their own homes.

Care of the elderly is slipping down the list of priorities as men and women submit to long grueling hours and chase impossible targets.

Declining family support is not the only factor that increases the vulnerability of the elderly in a developing country such as Pakistan. In many western countries, robust health-related social support systems are in place to ensure care for people who cannot afford exorbitant fees.

In the UK, for instance, acutely sick elderly who require temporary hospitalization get free treatment and food via the National Health Service (NHS), which is funded from compulsory taxation. Long-term hospital beds are available for elderly patients suffering from terminal illnesses. Moreover, there are residential hospices that offer palliative care, as well as free treatment and food. Although funded by charities, patients and their friends are encouraged to make donations to hospices, if affordable for them.

In Pakistan, on the contrary, health shocks frequently drain families of their hard-earned savings and expose them in heavy debts. And those who neither have savings nor ways of borrowing money simply die sooner.

"More than 73% of the population in Pakistan pays out-of-pocket to access healthcare," an internationally acclaimed public health specialist.

The absence of decent health care facilities for the elderly in public and private hospitals is a critical gap that needs to be bridged. While it would be over-ambitious to expect designated in-patient or community facilities for patients beyond the age of 65, efforts must be made to meet at least the barest minimum standards of care.

The nursing staff in most hospitals lacks the very basics of compassionate handling of the elderly. Psychosocial counseling remains a distant dream. Elderly patients are seen queuing up for hours for diagnostic tests or medical consultations, with hospital administrations unconcerned.

Pakistan's elderly make up only 7% of the population. Interventions that could provide them with a comforting environment do not require a mammoth investment. Whilst it is critical for the government to step up effective social support and protection for the elderly as it takes stock of its policy, it is also important that we revisit our changing societal values, which impact our homes, families, and loved ones.

Original Article

First Trimester Termination of Pregnancy – Role of Sublingual Misoprostol

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ABSTRACT

Objective: The objective of this study was to evaluate the efficacy acceptability and dose of misoprostol sublingually in the management first trimester pregnancy failure.

Study Design: Observational Study

Place and Duration of Study: This study was conducted in the Department of Obstetrics and Gynaecology at Peoples Medical College Hospital Nawabshah from 01.01.2010 to 31.12.2010.

Patients and Methods: A total 150 patients with the diagnosis of missed and incomplete miscarriage upto 13 weeks gestation. All eligible women who consented were counseled and given detail information protocol.

Results: A total of 150 patients with missed miscarriage 119 (79.33 %) and incomplete miscarriage 31 (20.66 %).The mean age group 28.34 years ,mean parity 4.79 and mean gestational age 8.61 weeks. Efficacy was 92 %, 127 (84.66 %) had complete miscarriage by the end of 7 days with 2 doses of misoprostol 600ug sublingually 3 hours apart. 23 (15.33 %) require 3rd dose of misoprostol and 11 (7.33 %) underwent surgical evacuation. Patients satisfaction was 94 % (141 patients).

Conclusion: Misoprostol prove with benefit of efficacy, safety and acceptability in first trimester pregnancy failure. In low resources countries achieve infection haemorrhage and uterine damage can for two commonly reported on consequences of post surgical care. Misoprostol treatment can prove to be a rewarding step towards reducing morbidity and mortality.

Key Words: Misoprostol, First trimester pregnancy termination, Sublingual route.

INTRODUCTION

Termination of pregnancy is one of the common procedures in gynaecological practice.

Medical management of early pregnancy failure is an effective, safe and cost effective alternative to surgical method and suitable for women not wanting hospital admission or unfit for general anaesthesia[1]. The synthetic prostaglandin, misoprostol (PGE1 analogue) has largely replaced all other technique for pregnancy[2].

Misoprostol, prostaglandin E1 analogue, is safe option and gaining popularity because of its uterotonic and cervical priming action. It is inexpensive and stable at room temperature. Sublingual route avoids first pass effect through the liver, has the shortest time to peak concentration that is 30 minutes as compared to 75 minutes in vaginal route and greatest bioavailability as compared to other routes, due to high vascularity of buccal mucosa. It also avoids painful vaginal administration and is more convenient to take and acceptable by women[3,4,5]. The main drawback is gastrointestinal side effects, shivering and hypothermia[5].

First trimester miscarriage is one of the most common complications of pregnancy occurring in 10 – 15 % of clinically recognize pregnancies[6].

South-Asia being highly populated resource constrained and underdeveloped region, holds almost one third (30 %) of world's maternal deaths and approximately 13 % of them are related to abortions and its procedures[7].

Different studies have evaluated efficacy of misoprostol in early pregnancy failure with success rate ranging from 13 – 100 % which is influenced by many factors as diagnosis sac size, and number of dose. Efficacy rate 90 % when compared to manual vaccum aspirator in two other study documented[8,9].

Misoprostol is useful for elective medical abortions, cervical ripening before surgical abortions, evacuation of uterus in case of embryonic or fetal death and induction of labour[10]. Misoprostol is widely available of low cost, stable at room temperature and easy to use for both patient and clinician make this an excellent treatment in low source setting[11,12].

The objective of performing this study was to evaluate the efficacy, acceptability and dose of sublingually in the management of first trimester pregnancy termination.

PATIENTS AND METHODS

This is observational study conducted in Obstetrics & Gynaecological Department at Peoples Medical College Hospital Nawabshah. A total of 150 patients with the diagnosis of missed and incomplete miscarriage up to 13 weeks were invited to participate into the study after taking informed consent. Diagnosis of missed miscarriage was made when Os was closed, nil or mild vaginal bleeding, an embryonic or no fetal cardiac activity seen on ultrasound. Incomplete miscarriage was diagnosed when there was history of passage of tissue

and or blood, Os was opened mild or moderate bleeding or an ultrasound showing fetal remnants.

Exclusion criteria, women with fever, haemoglobin less than 9 g/dl, heavy vaginal bleeding regarding emergency surgical evacuation, contraindication to prostaglandin therapy (Asthma, Uncontrolled blood pressure, Hypertension, Glaucoma, Cardiac and Renal disease).

All eligible women who consented were counseled and given detailed information about protocol. For incomplete abortion single dose of 600 µg was given sublingually. For missed miscarriage 600 µg of misoprostol was given sublingually and repeated after 3 hours and waited for 7 – 14 days until complete miscarriage. The patients were explained about side effects and were instructed to report if they have heavy bleeding. They were told that bleeding may start anytime and complete abortion take one to two weeks. In case of profuse bleeding explained us soaking more than 2 extra large sanitary pads an hour for more than 2 consecutive hours or bleeding continuously for two weeks, they were instructed to report back to hospital. In case of retained placenta of conception third dose of 600 µg is repeated sublingually and left to ward for a total of 14 days from the first dose. All women were followed up till complete abortion or 14 days. Acceptability was allowed by verbally asking the patient if they were satisfied with this treatment or unsatisfied.

RESULTS

A total of 150 patients with missed miscarriage 119 (79.33 %) and incomplete miscarriage 31 (20.66 %) uptil 13 weeks gestation were included in the study. Demographic characteristic of women with miscarriage (Table-I). The mean age is 28.34 years, mean gestational age is 8.61 weeks, mean parity is 4.79 and 139 women completely evacuated, remaining 11 underwent surgical evacuation of uterus thus the efficacy of sublingual misoprostol in our study is 92 %. 127 (84.66 %) women had complete miscarriage by the end of 7th day with two doses of 600 µg sublingual misoprostol 3 hours apart. 23 (15.33 %) patients were given third dose sublingual misoprostol as they came with retained products of conception at the 7th day.

Single dose misoprostol was given to all incomplete miscarriage and all of them had complete miscarriage in first 24 hours. Total 11 women underwent surgical evacuation and 2 due to heavy bleeding and remaining 9 were unsatisfied and could not wait larger and efficacy of sublingual misoprostol is 48.66 % in 24 hours of administration of drug and 30.66 % in 48 hours although majority of patients were from miscarriage. Total 2 women had heavy bleeding remaining had mild and moderate bleeding.

We also included women with history of previous cesarean section. We had 21 patients with previous one cesarean section and 7 patients with 2 cesarean sections who were given same dose of misoprostol another with no added complication.

Regarding side effects, only 18.66 % observed shivering, 11.33 % nausea, 4 % unpleasant taste and 3.33 % diarrhea.

Patients satisfaction was 94 % (141 patients) and only 9 (6 %) were unsatisfied who refused to wait larger for spontaneous complete miscarriage and opted for surgical evacuation on 3rd of treatment. Acceptability was 92.67 %, whereas 7.33 % does not like to choose method again.

Table No.1: Demographic Characteristic of Women With Miscarriage (n = 150)

Parity				
Parity	Frequency	Percent	Valid Percent	Cumulative Percent
1-3	19	12.7	12.7	12.7
4-6	41	27.3	27.3	40.0
>6	90	60.0	60.0	100.0
Total	150	100.0	100.0	

Gestational Age				
Gestational Age	Frequency	Percent	Valid Percent	Cumulative Percent
<2 weeks	36	24.0	24.0	24.0
7_13 weeks	114	76.0	76.0	100.0
Total	150	100.0	100.0	

Statistics (n = 150)			
Statistics	age	party	Gestational Age
Mean	28.3400	4.7933	8.6133
Median	28.0000	5.0000	9.5000
Mode	30.00	6.00	10.00
Std. Deviation	5.65190	2.68052	3.58930

Type of Abortion	No of Cases	Percentage
Missed abortion	119	79.33 %
Incomplete abortion	31	20.67 %

Table No.2: Frequency of women requiring different dose regimen (n = 150)

Outcome Measures	**No. of Cases**	**Percentage**
Induction to Delivery Time		
24 hours	73	49.67 %
48 hours	46	30.66 %
72 hours	21	14.00 %
96 hours	03	2.00 %
07 days	07	4.67 %
Dosage		
Single dose	31	20.67 %
Two doses	96	64 %
Three doses	23	15.33 %

Table No.3: Side Effects (n = 150)

Side Effects	No. of Cases	Percentage
Blood Loss		
Mild	87	58 %
Moderate	61	40.67 %
Heavy	02	10.33 %
Shivering	28	18.66 %
Nausea	17	11.33 %
Unpleasant Taste	06	4 %
Diarrhoea	05	3.33 %
Satisfaction		
Satisfied	141	94 %
Unsatisfied	09	6 %
Acceptability		
Yes	139	92.67 %
No	11	7.33 %

DISCUSSION

Misoprostol, a prostaglandin PGE1 analogue has cervical ripening and uterotonic properties thus making it is useful drug in obstetrics[3,13]. Misoprostol is widely available. It is of low cost and stable at room temperature. There are varieties of medical and surgical techniques for termination of pregnancy[14].

It is easy to use of both for the patient and clinician. It is thus excellent choice of treatment for use in low resources setting[9]. Uterine evacuation by medical methods reduces the morbidity associated with surgical intervention[1,15].

This study demonstrates the efficacy and safety of outpatient medical management of first trimester miscarriage. The use of two doses of 600 µg, misoprostol sublingually with followup for 7 – 14 days reduce the need of surgical evacuation by 94 %. In addition, this dose and route achieved 73 (49.67 %). Complete miscarriage in the first 24 hours and 30.66 % in 48 hours following therapy. We also found that women with spontaneous incomplete miscarriage were more likely to have complete expulsion after one dose of 600 µg sublingually than women with missed miscarriage. The higher patient satisfaction in our study also reflect successfully outcome which highlights the importance of counseling women before opting for medical management regarding side effects, waiting time of 7 – 14 days and needs surgical intervention in those who failed to successfully evacuate the uterus within this time frame.

The overall success rate for complete miscarriage in our study is 94 % which is comparable to similar studies reported from China and India. They used 600 µg of sublingually and vaginal misoprostol and reported an overall success rate of 87.5 % and 86 respectively[13,16], whereas Khatija et al[17] from Pakistan reported 92 % success rate single dose of sublingually misoprostol. Higher success in our study may be due to waiting time of 7 – 14 days as its is well recommended that waiting period of 7 days should be allowed to maximize the chance of success and reduce the number of unnecessary surgical interventions[13].

Two studies comparing a single dose of oral misoprostol 600 µg versus 600 µg two doses with a 4 hours interval showed no difference in efficacy between the two regimen[18,19] weeks et al used 600 µg of oral misoprostol and showed success rate of 96.3 %[19]. Different misoprostol alone regimen have been reported in literature for medical management of first trimester miscarriage. These studies are difficult to compare on different regimen and waiting time was used. WHO clinical guidelines 2007 clearly recommends 600 µg of g/L misoprostol only 2 doses 3 hours apart for the management of first trimester missed miscarriage with waiting periods of 7 – 14 days[20].

In our study, sublingual administration found side effects shivering 18.66 %, nausea 11.33 %, unpleasant taste 4 % and Diarrhoea 3.33 %. In another study, JS Bagrate[21] from South Africa reported 21 % whereas Tang OS et al[13] found 70 % incidence of diarrhea and 20 % found another study in Pakistan[22]. The unpleasant taste found 63 % in one study in UK[23], whereas one study in Pakistan found only 15 % cases[22]. Blood loss on reported by patient in our study was moderate 40.67 %, heavy loss was observed in only 10.33 % (2 cases). They were hospitalize and underwent surgical evacuation, remaining 58 % had mild bleeding reflect the safety of misoprostol in another study at Pakistan found heavy loss 6 cases and moderate in 75 %, 20 % cases had mild bleeding[22].

It appears that one regimen of 600 µg sublingually upto two doses has well tolerated by in patient which is not much increase in side effect. We have found that our medical regimen is associated with high degree satisfaction and acceptability. Wards and Grazin et al[24,25] also found high satisfaction in their study on medical management. The introduction of any new management intervention must also convince health providers that in addition to safety and tolerability, it might be acceptable to patient. We have found that our medical regimen is associated with high degree satisfaction and acceptability.

Medical management using misoprostol could revolutionize the existing treatment option of abortion. This method greatly improve access and service by enabling women to seek effective appropriate care at secondary and primary healthcare facilities with non surgical trend, providing it could be clean the burden on tertiary healthcare facilities economic resources because of its low costs as well as reducing the need to surgical supplies, stabilization and altering.

CONCLUSION

Misoprostol prove with benefit of efficacy, safety and acceptability in first trimester pregnancy failure. In low resources countries achieve infection haemorrhage and uterine damage can for two commonly reported on

consequences of post surgical care. Misoprostol treatment can prove to be a rewarding step towards reducing morbidity and mortality.

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Original Article

Frequency of Hepatitis B and C in Patients Reported at Al-Tibri Medical College & Hospital

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ABSTRACT

Objective: The aim of this study is to determine the frequency of hepatitis B and C in the residents of Malir district who reported to Al Tibri Medical College & Hospital.

Study Design: A Cross Section Prospective study.

Place and Duration of Study: The study was conducted in the Department of Medicine and Pathology of Al Tibri Medical College & Hospital from May 2010 to April 2011.

Materials and Methods: This study was based on the data of patients who reported to the hospital in a year. Pakistan is a developing country. On one side we have a population burden and on the other side communicable diseases. Viral Hepatitis is one of them. In general population the frequency of hepatitis B and C viral infection ranges from 8-15 %. Rapid Chromatography immunoassay and ELISA were the methods for the tests. The data was collected in a preset Performa and analyzed on SPSS version 16.

Results: Total of 2093 specimen were reported. Both hepatitis B surface antigen and anti HCV antibody were checked. Total number of persons screened were 2093. Out of them male were 963 and female were 1130. HBV were 124 positive cases while 426 were anti HCV positive. This showed that HBs antigen were 5.9 % while Anti HCV antibody were 20.35 %. Among HBs Antigen positive cases 61 % were males while 39 % were females and in Anti HCV antibody positive cases the females were 67 % while 33 % were males. Hence combined infection were 2.7%. Cases were divided into five groups according to their ages. The group of ages between 25 to 45 had maximum positivity.

Conclusion: The frequency of HBV and HCV in this particular area of our great province is quite high. This is the time to educate the general population of area so as to prevent the disease.

Key Wards: Hepatitis B virus , Hepatitis C virus, Gadap, Frequency.

INTRODUCTION

Hepatitis B virus and Hepatitis C virus were among the major health issues from the last one and half decade in our country. It is the major cause of the chronic liver disease and hepatocellular carcinoma. The prevalence of hepatitis B virus and hepatitis C virus in general population is 10% and 15% respectively[1] The World Health Organization[2], estimates show that there are 350 million people with chronic HBV and 170 million people with chronic HCV infection world wide. Hepatitis B causes 563000 deaths while 366000 deaths occurs from HCV. Some of these cases will finally end up in hepatocellular carcinoma.

HBV is a 42-nm hepadnavirus[3] with a partially double-stranded DNA genome, inner core protein and outer surface coat. There are eight different geno-types(A-H), which may influence the course of infection and responsiveness to antiviral therapy.HBV is usually transmitted by inoculation of infected blood and blood products or by sexual contact and is present in saliva, semen, and vaginal secretions. HBs Ag- positive mothers may transmit HBV at delivery, the risk of chronic infection in the infant is as high as 90%. HBV is found prevalent in men who sex with men and in injection drug users[4] but the greatest number of cases results from heterosexual transmission. The incidence has decreased by 75 % since 1980s. The groups at risk include patients and staff at hemodialysis centers, physicians, dentists, nurses and people working in clinical laboratory and blood banks. The incubation period of hepatitis B is 6 weeks to 6 months. The onset of hepatitis B is incidous. After an acute hepatitis B infection, HBV infection persists[5] in 1-2 % of immunocompetent adults but higher is number in immunocompromised adults and children. If HBV infection is acquired early in life and viral replication persists there may be 25-40 % chances of developing cirrhosis and hepatocellular carcinoma.

HCV is a single-stranded RNA[6] virus. There are six major genotypes of HCV which have been identified. In the past, HCV was responsible over 90 % of cases of posttransfusion hepatitis yet only 4 % of cases of hepatitis C were responsible to blood transfusions. Over 50 % of cases are transmitted by injection drug use. Body piercing, tattoos, and hemodialysis are also risk factor. The risk of sexual and maternal-neonatal transmission is low. Having multiple sex partners may increase the risk of transmission. Transmission via breast feeding has not been documented. In the developing world like Pakistan, unsafe medical practices are responsible for the huge number of HCV infected cases. Co-infection with HIV is 30 %. It increases the course of the disease. Incubation period average 6-7 weeks, initially there is a mild disease or asymptomatic but over 80 % chances of chronic

infection[7]. HCV infection may induce insulin resistance and increases the chances of type two diabetes mellitus. Considering Pakistan growing population with asymptomatic and unscreened people would really be a great burden on the health sector. Poor literacy rate, low socioeconomic status unhygienic condition and unsterilized equipment[8 9] and procedures were the main contributor for these results. The aim of this study is to determine the frequency of this big problem in the area of District Malir and is the real and original data.

MATERIALS AND METHODS

A cross sectional study was done in private hospital from May 2010 to April 2011 (12 months). All the cases above 18 years of age were screened for Hepatitis B surface antigen and Anti HCV antibody. The data were recorded on a preset proforma and analyzed through SPSS version 16. Tests were done on Rapid Chromatography immunoassay for qualitative detection of surface antigen of hepatitis B and Anti HCV Test were done on ELISA. The persons with known status for HBV or HCV infection were not included in this study and also who had taken treatment for chronic hepatitis were also not included in this study. The laboratory where those tests were performed is well equipped and qualified staff and doctors had performed those tests.

RESULTS

Total of 2093 cases were screened for both HB surface antigen and anti HCV antibody. Among the cases 83% were residents of the Gadap, 8 % were of Malir city, 5 % from Bin Qasim and 4 % were from Landhi Males were 963 and females were 1130. HBV were positive in 124 cases while 426 were anti HCV positive. This showed that HBs antigen were 5.9 % while Anti HCV antibody were 20.35%. Among HB surface Antigen positive cases 61 % males while 39 % were females and in Anti HCV antibody positive cases the females were 67 % while 33 % were males. The combined infections were 2.7%. Cases were divided into five groups according to their ages.

Table No. 1: HB Surface Antigen Positive Cases

Groups	Males	% of Cases Positive	Females	% of Cases Positive
18-25 Years	9	11.84 %	6	12.50 %
26-35 Years	24	31.84 %	13	27.08 %
36-45 Years	29	38. 15 %	17	35.41 %
46-55 Years	9	11.84 %	7	14.58 %
> 55 Years	5	6.57 %	5	10.41 %
Total	76	100 %	48	100 %

The Table No.1 showed the relative frequency in different age groups of the candidates in HBV surface antigen while Table No. 2 showed similar results of Anti HCV antibody positive cases. The groups of ages between 25 to 45 had maximum positivity. Female had more HCV while males had more HBV.

Table No. 2: Anti HCV Antibody Positive Cases

Groups	Males	% of Cases Positive	Females	% of Cases Positive
18-25 Years	35	25.17 %	45	15.67 %
26-35 Years	46	33.09 %	109	37.97 %
36-45 Years	27	19.42 %	89	31.01 %
46-55 Years	17	12.23 %	37	12.89 %
> 55 Years	14	10.07 %	7	2.4 %
Total	139	100 %	287	100%

DISCUSSION

Pakistan is a poor country and has many health issues. The health policies are not on mark and particularly in remote areas of Sindh. What factors really affect these do not fall within the scope of this article, but it provides an eye opening for the health officials of the local areas in particular and overall in general. This is a cross sectional study, conducted in a peripheral tertiary care hospital situated in a remote area of Sindh i.e. District Malir, is a thickly populated rural area with low literacy and poor socio-economic conditions.

The frequency of HCV is more than HBV [10]. The reason behind this is the development of the safe vaccine in HBV infection. More females were reported in this study as the cases were coming to hospital during day time and females reported to hospital easily than the males. The HBV was more common in males while HCV was more common in females. The frequency of HBV and HCV are comparable with other studies. It should be mandatory in every medical setup that these test will be for a patient having a minor or major surgery, with the availability of sterilized equipment and trained staff. [11]

The age ranging from 25-45 years had high prevalence for both HBV and HCV infections that was almost more than 50 % of the total.[12] The number of positive cases in older age group were less. The frequency of HBV surface antigen positivity in this study was 5.9 % while of Anti HCV antibody positivity was 20.35 %. The combined frequency was 2.7 %.

As it is a general review of the population of District Malir reported in Al Tibri Medical College & Hospital regarding HBV and HCV infection, the patients who turned out to be positive did not realize about the severity of their disease. The prevalence of our study of

HBV positive was comparable with other studies. In New Zealand, it was < 1 % , 2-4 % in Japan, 5-18 % in China, 15-20 % in Taiwan and in Sudan, it was 16.8 %. The prevalence of chronic HCV infection is < than 0.1 % in UK while 22% from Egypt, 38 % in Nigeria. These results are comparable with many studies. [13 14 15 16 17]

Now this is the proper time to take serious action regarding its prevention and proper sterilization of equipments[18] and making efforts to educate the common people of Pakistan about these hazards and its consequences. Make it sure[19 20] to screen all those who are either admitted or who visit the OPD.[11] Teach them the mode of transmission and give awareness to them.

CONCLUSION

The frequency of HCV infection is alarming and it should be taken seriously. The frequency is more than one fifth of the population. This area would be a reservoir for the future generation. This is the time to take serious action and implement preventive measures. It should make mandatory to vaccinate every Pakistani for HBV and educate about HCV infection.

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Original Article

Partial Edentulism Based on Kennedy's Classification

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ABSTRACT

Objective: The aim of this study is to investigate the distribution of the partial edentulism in general population according to Kennedy's classification.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted Isra Dental College OPD in Hyderabad from Feb 2010 to July 2011.

Materials and Methods: This is a cross sectional study carried out on 395 subjects, both males and females and belonging to age groups 35-50 years, completed during the period of one and half year. All patients' personal history was taken regarding their age and socioeconomic condition. Partial edentulism was recorded by visually examining the study sample.

Results: The results include the visual examination of 395 individual in which majority were males 246 (62 %), mostly belonging to the poor class , 231 (59 %) and in early forties 181(46%). There is high prevalence of Kennedy's class IV, 128(32 %) among sample then followed by Kennedys Class I 92(23.3%), II 76(19.2%) and III 50(12.7%). The association between partial edentulism according to Kennedy's classification with socio-demographic profiles of the sample is statistically significant (68, 17%; p=0.04).

Conclusion: In our study there is significant difference between gender and partial edentulism as more male patients visit the dental clinic for partial denture belongs to low income status and in 41-45 years age group.

Key Words: Kennedy's, partial edentulism, partial denture, prevalence, caries.

INTRODUCTION

Partial edentulism is the loss of some but not all natural teeth in either dental arch[1] and in many countries pattern of tooth loss has been evaluated in their population[2] .It has been proven that poor oral hygiene increases the incidence of tooth loss which have direct effect on the general health in the form of eating problems and weight loss[3]. The quality of life commonly affected by tooth loss; self consciousness and embarrassment restrict the social contact and communication[4]. The partial edentulism may also be related to complex behavioral and socioeconomic factors[5]. There are wide ranges of treatment options available to fix the problem of partial edentulism which broadly includes removable prosthesis and fixed prostheses [6].

The dental caries and periodontitis both are predominant reason for extraction among population and are directly related with tooth loss[7]. Moreover, combination of smoking and dental caries is also significantly contributed to partial edentulism[8]. It has been documented that partial edentulism was more common in females then in males[9]. Therefore, the objective of the study was to explore the study is to investigate the distribution of the partial edentulism in general population according to Kennedy's classification.

MATERIALS AND METHODS

A cross sectional study was conducted among 395 patients visiting Isra Dental College OPD in Hyderabad, from Feb 2010 to July 2011. Permission was granted by the research and ethical board of Isra University prior to the study. A close ended questionnaire consisted of two sections was designed to collect data from the participants. Section one includes questions regarding socio-demographics (age, gender, monthly income,) of respondents while section two examination of edentulism according to Kennedys classification by first author himself. Kennedy's classification system with Applegate's modification rules was used to determine pattern of partially edentulous arches.4 Modification areas were also included in the study. The socioeconomic status was evaluated from the data collected from monthly income. Participants were asked to mark the total monthly income below or above Rs. 15000. Those earning Rs. 15000 or below per month were considered as underprivileged class and those earning above Rs. 16000 were considered as privileged class. The study included both males, female's participants, aged between 35-50 years; Subjects were divided in three groups 35-40 years, 41-45 years and 46-50 years. The study excluded participants with mental health problems and handicapped. Data was analyzed using SPSS 17; frequency distributions of the sample were

calculated. Chi-squared test was applied to test the association between socio-demographics and Kennedys classifications. Level of significance was set to be p>0.05.

RESULTS

The result comprised of the responses of 395 males and females participants, included in the study sample. Table 1 show the frequency distribution of socio-demographics. There were 246 (62 %) males and 149(38%) females patients of age range from 35-50 years, divided into three groups of participants i-e 35-40 years 115 (29%), 41-45 years 181(46%) and 46-50 years 99(25%). Out of 395 participants, 231 (59 %) were belonging to underprivileged class while 164 (41%) were belonging to the privileged class.

Table No.1: Frequency Distribution of Socio-Demographics

	Number of Individuals (n)	Percentage (%)
Socioeconomic Profile		
Poor Class	231	59
Middle Class	164	41
Gender		
Male	246	62
Female	149	38
Age		
35-40 years	115	29
41-45 years	181	46
46-50 years	99	25
Total	395	100

Table No.2: Associations of kennedys classifications with sociodemographic profile

Kennedys Classification	Gender n (%)		socioeconomic status n (%)		AGE GROUPS (YEARS) n (%)		
	Male	***Female***	***Poor Class****	***Middle Class***	***35-40***	***41-45***	***46-50***
Class I	54 (13)	38 (10)	64 (16)	28 (7)	33 (8)	42(11)	17 (4)
Class I (MOD)	16 (4)	10 (2)	16 (4)	10 (2)	7 (2)	11(3)	8 (2)
Class II	47 (12)	29 (7)	42 (11)	34 (9)	20 (5)	38(10)	18 (5)
Class II (MOD)	8 (2)	6 (1)	4 (1)	10 (2)	6 (1)	5 (1)	3 (1)
Class III	33 (18)	17 (4)	30 (8)	20 (5)	11 (3)	22 (6)	17 (4)
Class III (MOD)	5 (1)	4 (1)	7 (2)	2 (0.5)	1 (0.3)	6 (1)	2 (0.5)
Class IV	83 (21)	45 (35)	68 (17)	60 (15)	37 (9)	57 (44)	34 (27)

*P<0.05

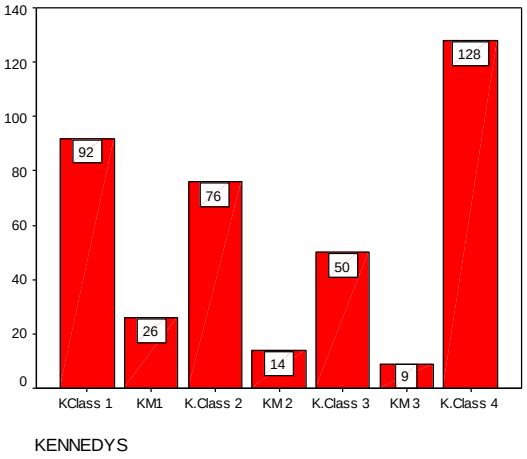

Figure No.1: Frequency Distribution of the Kennedys Classification

The Table 2 shows the association of Kennedy's classification with socio-demographics profile of the participants. The results showed that the partial edentulism were more in male patients than females and the prevalence of partial edentulism was high in age group 41-45 years. Moreover, partial edentulism was found to be high among underprivileged (40%) than privileged group. The high prevalence of Kennedys class IV is statistically significant in males 83(21%) in their early forties 57 (44%) with poor socioeconomic status (68, 17%; p=0.05).

Results illustrates in Fig 1 explains the frequency distribution of the Kennedy classification. According to that, Kennedy's class IV, 128(32 %) has highest prevalence among all classes, then followed by Kennedys Class I,92(23.3%), class II,76(19.2%) and class III,50(12.7%), while in Kennedys class I modification 26(6.6%), class II modification 14(3.5%)and class III modification9(2.3%).

DISCUSSION

The results of this non probable purposive study may not be representative of the population at large. Hence, its use can only be limited to the study population of particular area. A randomized population based survey may be able to present a better picture among Pakistanis. The table 1 explain the frequency distribution of socio- demographics that the more male patients 246 (62%) were partially edentulous than females 149 (38%). These results are in accordance with a study, as they found significant gender differences in edentulism, more males becoming edentulous than females.[8] while another study also support this study findings as they were also found more male patients with an average 2.37 requires

denture than females, an average of 2.29, with a small difference.[10]

Our results found maximum no of patients 181 (46%) in the 41-45 years age group, followed by 35-40 years age 115 (29 %) and least no 99 (25%) in 46-50 years with mean age of 45.8, nearly same results were documented in a Pakistani study with mean age of 35.3 ±9.5 years in their male participants.[11] and other Pakistani study also documented mean age of the patients was 43 years. [12]

Our study agreed with these two mentioned studies as we also have two types of subjects, poor class and middle class, the percentage of low income people (poor class) 231 (59%) have high demand of removable partial dentures than the middle class 164 (41%). Where as a Nigerian study documented significant association between partial edentulism with lower education level and lower socio-economic group ($p < 0.001$),[13] also an Indian study observed that the lower and middle income peoples exhibited a greater proportion of partial edentulism (85.3 %, 83.5%) than higher income people (66.1 %).[14]

In present study Kennedy's class IV was the most common class 32.4%,followed by Kennedy's class I (23.3 %) and class I modification I patients were (6.6%),than Kennedy's class II (19.2%). Kennedy class II modification II was (3.5%) and last category of the patients was Kennedy's class III (12.7 %) and class III modification 2 was (2.3) less number of patients in last two categories. Where as many studies documented the most commonest was the class III, as a Jordanian study investigated total 200 patients (152 male, 48 females mean age 44.5 years) and class III was the most common encountered in maxilla (47%) and in the mandible (45%).[15] same a brazil study established edentulism more in 21-40 years age (68.9%), and Kennedys class III (57.3%) was commonest and Kennedy's class IV (26.2%) was second common among all types.[16] where as our results shows the class IV is the commonest one class.

Table 2 explains the associations of Kennedy's classification with socio-demographic profile as Kennedy's class IV is more pronounced in male patients 83

(21%) belongs to poor class 68 (17%) in their middle age group 41-50 years 57 (44%) then in the class 1 males were 54 (13%) from poor class 64 (16%) and maximum 42 (11%) in 41-50 years age group, Class II and class III shows the 47 (12%) and 33 (18%) respectively and again maximum patients related to poor42(11%), 30 (8%) respectively and in the 41-50 years age groups, in class I modification males were 16 (4%) ,in class II modification 8 (2%) mostly belongs to middle class in the 35-40 years age group while in class III modification more males 5 (1%) all belongs to poor class 7(2%) in 41-50 years age group.

This may draw attention that the loss of tooth in an early age is predisposed to their poor oral hygiene as the eruption time of lower anterior teeth are earlier in the life and loss of tooth in this area is common due to periodontitis, gum recession, and trauma, less attention towards conservative treatment and low socio-economic status .

Partial edentulism was most commonly treated with removable partial dentures and only few patients were treated with fixed partial dentures in both jaws.

CONCLUSION

The prevalence of partial edentulousness linked with gender, socioeconomic condition as it is a big problem for people as they feels difficulty in socialization and problem in mastication. Esthetic is the main interest of females but males are also feels difficulty in socialization if they have anterior partial edentulism and this is the main reason Kennedy's class IV is the commonest among all classes followed by Kennedy's class III, Kennedy class II and finally class I. Male edentulous ratio is higher than females and low income group had more demand of removable partial denture.

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Original Article

Vitamin-E: Anti-Ulcer Activity; Beyond the Antioxidant Functions

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ABSTRACT

Objective: To evaluate the anti-ulcer activity of vitamin-E on caecal ulcerogenicity of Diclofenac sodium in Albino rats.

Study Design: A prospective experimental study

Place and Duration of Study: Department of Anatomy, Basic Medical Sciences Institute, Jinnah Post Graduate Medical Centre Karachi during 2003.

Materials and Methods: Diclofenac sodium and Vitamin-E were administered to Albino Rats separately and simultaneously at a dose of 2 mg/kg body weight (for each drug) orally once daily for two weeks. These animals were sacrificed, Caeca were identified and removed, opened along mesenteric border and examined under dissecting microscope for dilatation of the blood vessels, blood streaks and hemorrhagic areas. The caeca were fixed in 10% formalin, Embedded in paraplast, 4 um thick sections were cut on rotary microtome, stained with Haematoxylin and eosin stains. The histomorphological Features of caecal mucosa were compared with those in the control animals and analyzed statistically.

Results: The study revealed that simultaneous use of vitamin-E administration with (NSAIDs) produced Anti-ulcer activity in caecal ulcers of albino Rats.

Conclusion: The results suggest that vitamin-E produced anti-ulcer activity in Caecal ulcers of albino rats.

Key Words: Vitamin-E, Diclofenac sodium, Antiulcer activity, Caecal ulcer, Albino rat.

INTRODUCTION

Although vitamin-E was discovered nearly 85 years ago[1], the search for its biological function continues. Whereas the antioxidant function of Vitamin-E in vivo is no doubt crucial, there is a growing body of evidence that RRR-a-tocopherol may exert non-antioxidant effects on various aspects of cell metabolism. Vitamin-E, a potent peroxyl radical scavenger, is a chain breaking antioxidant that prevents the propagation of free radical damage in biological membranes[2,3]. Vitamin-E is the collective name for eight naturally occurring molecules, four tocopherols and four tocotrienols. Tocotrienols differ from tocopherols in that they have an unsaturated phytyl side chain; the four forms of tocopherols and tocotrenols differ in the number of methyl groups on the chromanol nucleus(α-has 3,β- and γ-have 2,whereas δ-has1).The biological activity of the various vitamin-E forms roughly correlate with their anti-oxidant activities; the order of relative peroxyl radical scavenging reactivities of α-, β-, γ-, and δ-tocopherols (100, 60, 25, and 27 respectively[4] is the same as the relative order of their biological activities (1.5, 0.75, 0.15, and 0.05 mg/iu respectively, determined by using the classic fetal resorption assay in rats.[5]

Upon closer scrutiny, the relation between antioxidant and biological activities breaks down. α-tocotrenols has only one third the biological activity of α-tocopherol[5,6] yet it has higher[7]or equivalent[8] antioxidant activity. A vitamin-E analog [2,4,6,7-tetramethyl-2-(4', 8', 12'-trimethyltridecyl)-5-hydroxy-3,4-dihydrobenzofuran] with equivalent biological activity to RRR-a-tocopherol[9] has 1.5 times the antioxidant activity[10]. Furthermore, synthetic vitamin-E (all-rac-a-tocopherol) contains equal amounts of eight different sterioisomers of α-tocopherol that have equivalent antioxidant activity, but each of which has a different biological activity[11].The biological activities of the 2-S forms are generally lower than the 2-R forms[11].Overall, the highest biological activity is found in molecules with three methyl groups and a free hydroxyl on the chromanol ring and the phytyl tail meeting the ring in the R-orientation. This specific requirement suggests specific interactions of vitamin-E with proteins and perhaps with other molecules, such as DNA.

This study was designed to evaluate the anti-ulcer activity of Vitamin-E on caecal ulcers, induced by diclofenac sodium (NSAIDs) in albino rats.

MATERIALS AND METHODS

Seventy-five albino rats were used in this study, which were obtained from Animal House of Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi. All were male, 20 weeks of age, weighing 180—200 grams, looking active and healthy. These animals were housed in the experimental room of Animal House maintained on balanced laboratory diet and water ad libitum with 12 hours light and dark cycle. Seventy-five animals were divided into three equal Groups; A, B and C, each comprising of 25 animals. Group 'A' animals were given Diclofenac sodium

(developed in Novartis Pharma Pakistan Ltd) at a therapeutic dose of 2 mg/kg/ body weight orally once daily for 2 weeks[12]. Group 'B' animals were given simultaneously Vitamin-E at a dose of 2mg/kg/body weight orally once daily, 30 minutes before administration of Diclofenac sodium (2 mg/kg/body weight) orally once daily for 2weeks[13]. Group 'C' animals acted as control and were given normal saline (equal volume of dose given to groups 'A' and 'B') orally Once daily for 2 weeks.

All the rats were sacrificed on day 15th of the experiment by giving deep ether Anesthesia and were operated to obtain their caeca, which were fixed in 10% Formalin, embedded in paraplast and 4 um thick sections were cut on rotary microtome. These sections were stained with Haematoxylin and eosin reagents. The histomor-phological features of caeca in all the groups were observed with respect to total epithelial cell count per unit area (0.0324 mm^2/field) and mucosal thickness was measured by micrometry and the data was subjected to statistical analysis. Student "t" test was employed to see the significance of results.[14]

RESULTS

The animals in Group 'A' looked slow and weak during last 2-3 days of experimental period. They appeared lethargic, their response to stimuli was sluggish and food intake was decreased as compared to animals of Group 'B' and 'C'.

Table No.1: Comparison of Mucosal thickness (µm) and Total epithelial cell count per unit area between Groups – A, B and C during experimental period.

Groups	Mucosal thickness (µm)	Total epithelial cell count	
		NFO	
A(n=25)	52.562 ± 1.436*	25	441.655±1.963*
B(n=25)	149.062±0.439**	25	576.256±1.130**
C(n=25)	151.375±1.126	25	578.851±1.753

Statistical Comparison

Groups	P Value	Significant / Non-significant
A vs B	< 0.001*	Highly Significant ↓
A vs C	< 0.001	Highly Significant ↓
B vs C	> 0.05**	Non-significant change

Note: Values are given as mean ± standard error of mean.

* P ‹ 0.001 (Highly significant)

** P › 0.05 (Non-significant)

Key: NFO = No; of field observed (0.0324 mm^2)

µm = Micrometer

Under light microscope the animals of Group 'A' showed epithelial mucous secreting cells in mucosa disrupted and exfoliated at places with moderate degree of pyknotic nuclei. Inflammatory exudates including numerous lymphocytes, plasma cells, neutrophils and degenerated cells were observed in abundance within and around the erosions/ulcers, as shown in Figure -1.

The Group 'B' animals showed almost intact histological structure without any change in caecal mucosa with decreased lymphocyte infiltration and degenerating cells, as shown in Figure-2. While Group 'C' control animals showed intact histological structure without any change in caecal mucosa, as shown in figure – 3.

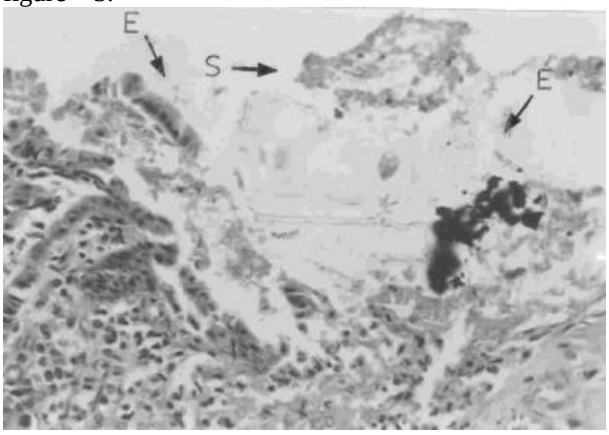

Figure No.1: Photomicrograph of 4 um thick paraplast section of caecal mucosa stained with H & E in Diclofenac sodium treated (Group 'A') albino rat, showing an erosion, marked against (E→) with inflammatory exudates and sloughing of surface epithelial cells (S→) under high power. Objective, x416

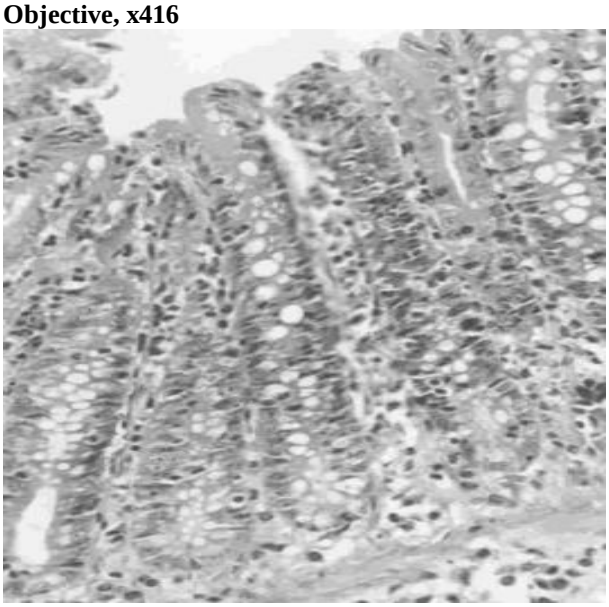

Figure No.2: Photomicrograph of 4 um thick paraplast section of caecal mucosa Stained with H & E in Diclofenac sodium and Vitamin – E (group-B) treated albino rat, showing surface epithelial cells comparable with normal control under high power Objective, x416.

The mean values of the mucosal thickness in group 'A', 'B' and 'C' were recorded as 52.562±1.436, 149.062±

0.439 and 151.375±1.126 µm respectively, as shown in the Table-1. A remarkable highly significant (P <0.001) decrease in mucosal thickness in Group 'A' was observed when the difference of mean was compared with Group 'B' and 'C' while no significant (P>0.05) change was observed when the difference of mean in Group 'B' was compared with animals in control Group 'C'.

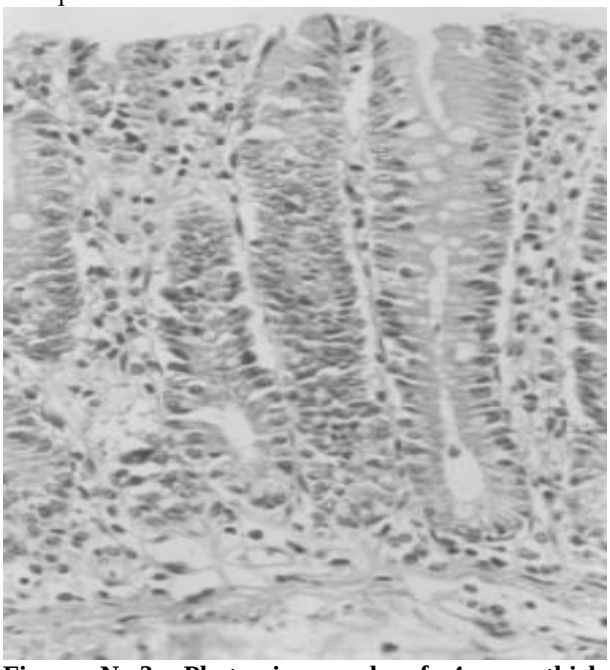

Figure No.3: Photomicrograph of 4 um thick paraplast section of caecal mucosa Stained with H & E in normal control (group-C) treated albino rat, showing entire mucosal thickness under high power Objective, x416.

The Mean values of Total epithelial cell count per Unit area in Groups 'A', 'B' and 'C' were recorded as 441.655±1.963, 576.256±1.130 and 578.851±1.753 respectively, as shown in the Table-1. A highly significant P <0.001) decrease in total epithelial cell count per unit area in Group 'A' was observed when the difference of mean was compared with Group 'B' and 'C'. While no significant (P>0.05) change was observed when the difference of mean in Group 'B' was compared with animals in Group 'C'.

DISCUSSION

The present study was designed to observe the anti-ulcer activity of vitamin-E when used simultaneously with the Diclofenac sodium (NSAID) in caecal mucosa of albino rats. The diclofenac sodium administered in a normal therapeutic dose of 2 mg/kg body weight, once daily orally for 2 weeks.[12] After treatment with diclofenac sodium (NSAID) in animals of Group 'A', general behavior changed to ill, sluggish and decreased food intake which may be attributed to unwanted effects of diclofenac sodium toxicity. In this context our results are in agreement with Gabriel et al[15], Bjarnason et al[16], and graham et al[17] who stated that administration of Diclofenac sodium was associated with increased gastrointestinal toxicity include mild dyspepsia or cachexia as well as more serious gastrointestinal reactions such as ulceration, bleeding, perforation and other events leading to hospitalization or death.

On microscopic examination of caecum revealed decreased mucosal thickness with decreased total epithelial cell count per unit area. These changes are in conformity with the Studies by Van-kolfshoten[18], Kaufman[19], Graham et al[17] and Manocha[12]. A highly significant (P <0.001) decrease in mucosal thickness was observed which may be attributed to the injurious effect caused by Diclofenac sodium (NSAID) which might have resulted into onset of the demolition with extensive exfoliation of surface epithelial cells and ulceration. At places, mucosal lining of caecum showed necrosis which according to Kumar et al[20] resulted most commonly from sudden severe ischemia due to irreversible injury to cells.

A non-significant (P>0.05) change in mucosal thickness in Group 'B' was observed, which may be attributed to anti-ulcer activity of vitamin-E, as vitamin-E reduces the damaging effect of NSAIDs on the gastro-duodenal mucosa of rat with ulcers thus normalizing the phospho-lipid contents by decreasing lipid per-oxidation (LPO) markedly. It is suggested that LPO may be involved in the pathogenesis of ulcer and that factors attenuating the process of LPO may prevent ulcerogenesis.[21,22]

Our results are in complete agreement with Tariq[23] who found that pretreatment of animals with vitamin-E produces a significant inhibition of gastric lesions induced by NSAIDs. An increase in synthesis of prostaglandins and a high level of glutathione in tissues of vitamin-E treated animals have been suggested as a possible mechanism of anti-ulcer activity of vitamin-E.

A highly significant (P <0.001) decrease in total epithelial cell count per unit area in Group 'A' was observed, which may be attributed to decrease in secretory activity and flattening of cells due to ulcerogenic effect on cell morphology, the mucin content in goblet cells become depleted. Our results are in complete agreement with Lee[24] who found that the crypts showed substantial goblet cell depletion with diclofenac sodium, the inflammatory changes in which both plasma cells and lymphocytes participated were accompanied by more severe reaction and even crypt dissolution.

A non-significant (P>0.05) change in total epithelial cell count per unit area in group-B was observed, which may be attributed to anti-ulcer activity of vitamin-E, which when administered simultaneously produced these changes.

On microscopic examination of the caecal wall of Group 'C' animals, mucosal thickness and the total epithelial cell count per unit area were normal.

CONCLUSION

These results strongly suggest that Diclofenac sodium causes severe caecal ulcers, which could be prevented (as an anti-ulcer activity) by simultaneous administration of vitamin-E in albino rat.

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Original Article

Number of Human Segmental Arteries in Local Population

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ABSTRACT

Objective: To investigate the variations in the total number of segmental arteries in human kidneys obtained from cadavers of the local adult population.

Study Design: Observational Study.

Place and Duration of Study: This study was conducted at Anatomy Department of University of Health Sciences, Lahore, for a period of one year from October 2006 to October 2007.

Materials and Methods: Forty four adult human kidneys were obtained after autopsy; they were randomly divided in two groups A and B of right and left kidneys respectively. Simple blunt dissection and corrosion cast techniques were used to study the number of segmental arteries. Statistical analysis was carried out by using SPSS version 16.0 and STATA version 8.0.

Results: Segmental arteries were present in 100% of specimens of groups A and B; variations were seen in the number of segmental arteries of both groups.

Conclusion: The segmental branches of renal artery in local population showed variations different from those reported in the earlier work carried out in other countries.

Key Words: Kidneys, Segmental arteries.

INTRODUCTION

Recent advances and refinements in renal surgery as well as radiological interventional procedures have revived interest in renal arterial anatomy.[1,2] The vascular pattern of the kidney had been the topic of repeated anatomical investigations and the variations of renal arteries are considered critical issues of which the surgeons should have thorough knowledge.[3,4]

Renal arteries arise from abdominal aorta and supply the kidneys through a number of subdivisions. Near the renal hilum, each renal artery divides into anterior and posterior divisions (presegmental arteries), which further divide into segmental arteries supplying the renal arterial segments.[5-7] On the basis of arterial distribution, five segments of the kidney have been described and were named as apical, upper, middle, inferior (lower) and the posterior segments.[5,8]. Segmental artery clamping is anatomically feasible, it minimizes the number of nephrons exposed to potential ischemic injury and its accessibility may be a factor for choosing laparoscopic surgical approach; precise hilar dissection, including dissection of the segmental arteries has been safely performed on routine basis. If access to a segmental artery is challenging, presegmental arterial ligation can still spare most of the kidney from an ischemic challenge.[9] Familiarity with the possible variations in the renal arterial pattern is especially important for the surgeons dealing with kidney transplantation, various endourologic procedures and innumerable interventional techniques.[10-12]

MATERIALS AND METHODS

Forty four unclaimed adult human cadaveric kidneys were obtained from forty four cadavers from the Forensic Medicine Department of King Edward Medical University, Lahore. The kidneys were randomly divided into two groups, A and B, having right and left kidneys respectively; twenty two specimens were present in each group (n=22). The kidneys were irrigated with normal saline for flushing out of blood and formalin from the organ.[13,14] The segmental branches of renal arteries were studied by using simple blunt dissection and corrosion cast technique. After performing blunt dissection, the renal artery and its branches were painted with red oil paint. Batson's No. 17 corrosion kit (Polysciences) was used to make the renal arterial corrosion cast.[15] For maceration purpose, the kidney was placed in 20% solution of potassium hydroxide in a glass jar at room temperature; the amount of potassium hydroxide solution used was two to three times the volume of the renal mass.[14,16-19] After about ten days, the macerated tissues were removed; the specimen was washed with tap water and air-dried. The exclusion criteria consisted of: presence of renal abnormalities on gross inspection, evidence of renal trauma or renal surgery, and presence of abdominal growths. [17,20-24]

The statistical analysis was carried out using computer software Statistical Package for Social Sciences (SPSS) version 16.0 and STATA version 8.0. The significance of the data between the groups was calculated by Pearson Chi-square test and Fisher exact test; the

association was regarded statistically significant if the 'p' value was <0.05.

RESULTS

Variations in the total number of segmental arteries were observed. Segmental arteries were present in all the specimens of groups A and B. Total number of segmental arteries was 346, 176 in group A and 170 in group B. Although observations were observed in the number of segmental arteries in both the groups, no statistically significant association was found between the two groups (p value>0.05) (Figure I).

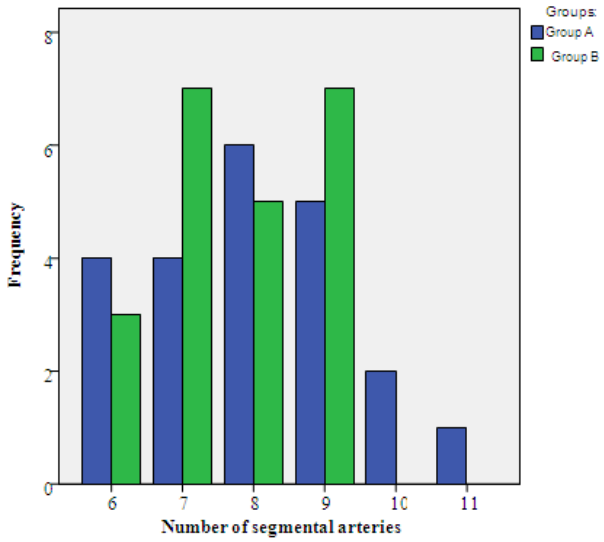

Figure No.I: Diagram showing variations in the number of segmental arteries in groups A and B.

DISCUSSION

The renal arteries are considered as an important anatomical landmark by all the anatomists, surgeons and radiologists dealing with the aortic and renal surgeries.[10] The present study gave the data for the variations in the total number of segmental arteries in right and left human cadaveric kidneys. In the current study, the segmental branches of renal artery showed high variability in their total number, which varied from six to eleven. These findings were consistent with the observations made by Kosiński and Oszukowski, in which two hundred corrosion casts of renal arteries demonstrated high variability in their origin, ramifications and the area of renal parenchyma supplied;[25] they showed difference in total number of segmental arteries.

Association between groups A and B in the total number of segmental arteries was statistically insignificant. The realization of the segmental nature of the branches of renal artery has led to the attempts of putting the partial resection of kidney on a rational basis.[26] Extensive hilar dissection with selective renal presegmental or segmental vascular occlusion may serve as another tool in the renal surgeon's armamentarium.[9] According to Moore, the manner in which the renal artery divides into its primary branches (segmental arteries) is variable and deviates markedly from the typical anterior and posterior branches described earlier.[27]

The variations of the branches of renal artery are important for various operative procedures like renal transplants, incision of renal pelvis, creation of a transcutaneous passage for nephroscope insertion, vascular reconstructions as well as constructive renal surgery.[25] The present study showed differences in the number of segmental arteries present in different specimens with a statistically non-significant association between the two groups. However, the present findings were consistent with the typical arterial pattern set by Graves and other researchers who found that segmental arteries originating from the presegmental branches of renal artery showed comparable pattern of supplying the apical, upper, middle, inferior and posterior renal segments and are variable in number. This difference could be explained on the basis of geographical and ethnical variations.

CONCLUSION

The segmental branches of renal artery in local population showed variations different from those reported in the earlier work carried out in other countries.

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Original Article

Protective Role of Melatonin on Streptozotocin induced Renal Damage in Albino Rats

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ABSTRACT

Aims and Objectives: This study was designed to evaluate the protective role of melatonin on the morphology of proximal convoluted tubules (PCT) of albino rats made nephrotoxic by a chemotherapeutic drug like streptozotocin (STZ).

Study Design: Prospective experimental study.

Place and Duration of Study: This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Post graduate Medical Centre (JMPC), Karachi, for 6 weeks from March to April, 2012.

Materials and Methods: 60 male albino rats were divided into 4 groups, containing 15 animals each. Group A was treated as control, groups B & C received 37 mg/kg STZ Intraperitoneally (I/P) once at the start of experiment, whereas group C additionally received 10mg/100 ml of melatonin (MEL) 3-days prior to STZ administration, and group D received only MEL at the same dose. Serum glucose was measured weekly. The kidneys were processed for histological examination and periodic Acid Schiff Haematoxylin (PAS-H) stained sections were viewed under the light microscope for detailed morphological examination of the proximal convoluted tubules.

Results: The microscopic examination revealed marked epithelial, cytoplasmic and nuclear changes in the P.C.T. of STZ treated group B & a significant reduction in the severity of these changes in MEL treated group C. Serum glucose was significantly increased in both group B and C.

Conclusion: The results of the investigation indicated that MEL administration suppressed the progression of renal injury induced by nephrotoxic drugs like STZ. It could not decrease STZ induced hyperglycaemia, but it did prevent the histopathological damage of the P.C.T. So dietary supplementation of MEL could be an easy and inexpensive method of protecting cancer patients from renal damage caused by chemotherapy induced oxidative stress.

Key Words: Streptozotocin, Melatonin, Nephrotoxicity, Oxidative stress, Oxygen Free Radicals, Reactive Oxygen species, proximal convoluted tubules.

INTRODUCTION

Medications commonly used in patients with cancer are notoriously nephrotoxic. The major groups of agents causing acute tubular toxicity are antibiotics, NSAIDS and chemotherapeutic agents. The proximal renal tubular cells vulnerability to the direct toxic action of chemicals is largely due to the role played by this portion of the nephron in absorption and secretion[1].

Nephrotoxicity is intrinsic to the pharmacological effect of certain anticancer drugs. Because antineoplastic agents have a narrow therapeutic index, the amount of drug required to significantly reduce tumour burden usually induces significantnephrotoxicity. Philosophically, greater toxicity is acceptable for curative therapy as opposed to palliative therapy[2].STZ is amongst one of the most nephrotoxic chemotherapeutic compounds in frequent use for the treatment of pancreatic islet cell carcinoma and carcinoid tumors[3]. The effects of STZ on different organs have been extensively studied. It is diabetogenic, hepatotoxic, nephrotoxic and also causes gastric ulceration[4].

Renal toxicity is the major dose limiting side effect of STZ[5]. The site of injury involves both the glomerulus and tubules, based on histologic changes[5]. By producing hyperglycaemia and hypoinsulinemia, STZ alters various metabolic and enzymatic functions of kidney, resulting in various pathologic lesions[3]. Formation of reactive oxygen species (ROS) is thought to be a mediator of the cytotoxic actions of STZ[6]. Organisms have developed several defence mechanisms to protect their cells against ROS. Such mechanisms include use of antioxidant enzymes and antioxidant molecules such as vitamin C, E and flavonoids.

Antioxidants are compounds that either reduce the formation of free radicals or react with and neutralize them. However, when a condition of oxidative stress establishes, the balance between free radicals production and the level of antioxidant molecules tilts towards excess of free radicals, and the defence capacities against ROS become insufficient.Melatonin (N-accetyl-5 methoxytryptamine), the chief secretary product of the pineal gland, is a multi-facetted free radical scavenger and a strong antioxidant[8]. It breaks down many free radicals, such as highly toxic hydroxyl and peroxyl radicals and oxygen free radicals (OFR). Melatonin can penetrate all the morphophysiological barriers in the human body due to its lipophilic and hydrophilic characteristics[9]. Thus MEL can effectively protect cell walls, organelles and nuclei from damage by free radicals. MEL functions as a modulator of

sleep, sexual behaviour, immune functions and circadian rhythm. Moreover, MEL has a potent ROS scavenger activity chiefly because of its capacity to act as an electron donor[10]. It decreases inflammation and impedes the progress of tissue edema[9]. It inhibits the accumulation of neutrophils in the damaged renal tissue[11].

In the light of the proceeding statements, this study was designed to study the protective role of MEL on the morphology of P.C.T. under the light microscope in albino rats made nephrotoxic by STZ. The effects of these drugs on serum glucose levels were also monitored.

MATERIALS AND METHODS

This study was conducted in the department of Anatomy, BMSI, JPMC,Karachi for a period of 6 weeks. In this study, 60 healthy male albino rats, 90-120 days old, weighting around 250-290 gm were obtained from the animal house of BMSI and divided into 4 groups, each group containing 15 animals.They were kept in propylene cages, equipped with drinking water bottles and wood chip floor bedding under laboratory environment. Serum glucose of all the animals was determined by a glucometer from the tail vein.

Group A was taken as control. The animals of group B and C were fasted overnight and administered STZ I/P in a dose of 37 mg/kg[12]dissolved in 1 ml of citrate buffer at 4 PH, only on the first day of the experiment. Group C additionally received 10 mg/100 ml[13] of MEL.Group D received the same amount of MEL in drinking water. The water bottles were covered with aluminium foil to prevent degradation of MEL by sunlight. Clean water bottles and freshly prepared MEL solutions were provided each day. Serum glucose of Group B and C animals was closely monitored throughout the experimental period. They were sacrificed at the end of treatment period the abdomen was opened by a midline Incision. Both the kidneys were exposed, dissected out and they were fixed in buffered neutral formalin for 24 hours. After thatthey were kept in 70% alcohol overnight, dehydration of the tissues was done with ascending strength of alcohol, cleared in xylene and infiltrated with paraffin at 59 degree. 5microns thick paraffin embedded longitudinal sections were made and stained with PAS-H for a detailed morphological examination of the P.C.T underlight microscope.A minimum of 10 fields of each kidney slide were examined and scored semi quantitatively for severity of changes. The scoring was done as none (-) mild (+), moderate (++) and severe (+++).

RESULTS

Group A: The lining epithelial cells of the P.C.T were regularly arranged on an intact and well defined basement membranes and distinct brush borders (fig-1). The mean values of serum glucose were 88.06± 5mg/dl (Table-1) and no lesions were observed upon Pathological grading (Table-2).

Group B: Most of the P.C.T. showed dilatation with severe sloughing and degeneration, while others showed shrinkage in size with necrotic changes (Fig-2) Most of the cells showed vacuolated appearance obscuring cytoplasmic details. The brush borders and basement membranes were highly discontinuous and distorted (Fig-2). The mean values of serum glucose were 379.12±15mg/dl, which were highly significant as compared to control (Table-1) Diffuse lesions were observed upon grading of the tubular damage (Table-2).

Group-C: There was an overall improvement and preservation of the morphology of P.C.T. as compared to group B(Fig-3). Most of the cells had well defined and intact brush borders and basement membranes. The mean values of serum glucose (360.18±7 mg/dl) were highly significant as compared to control group, high lighting the insignificant effect of MEL on serum glucose. The extension of tubular injury was significantly reduced by MEL (Table-2).

Table No.1: Mean*Serum glucose levels in different experimental groups of albino rat.

Groups	Serum Glucose (mg/dl)
A (Control)	88.06 ± 5.12
B (STZ)	379.12 ± 15.29**
C (STZ + MEL)	360.18 ± 7.36**
D (MEL)	84.02 ± 5.02

Each value is mean ± S.E.M. for 15 rats in each group
* Significant P < 0.01
** Highly Significant P < 0.05as compared to control.

Table No.2: Grading ofhistological changes ofP.C.T in different groups of albino rats

S.No	Lesions of P.C.T.	GROUPS			
		A	B	C	D
1	Degeneration of Tubular Epithelium	-	+++	+	-
2	Tubular Dilatation	-	++	+	-
3	Cytoplasmic Vacuoles	-	+++	+	-
4	Distortion of brush border membrane	-	+++	+	-
5	Distortion of basement membrane	-	+++	+	-
6	Interstitial inflammation	-	++	+	-

Key to Scores:
- No Lesion observed
+ Mild lesion observed
++ Moderate lesion observed
+++ Severe lesion observed

Group-D: Normal morphology of the P.C.T. was observed (Fig-4), same as control group (Fig-1). The mean values of serum glucose were similar to the

control group (table-1) and no lesions were observed upon grading of the tubular damage (table-2).

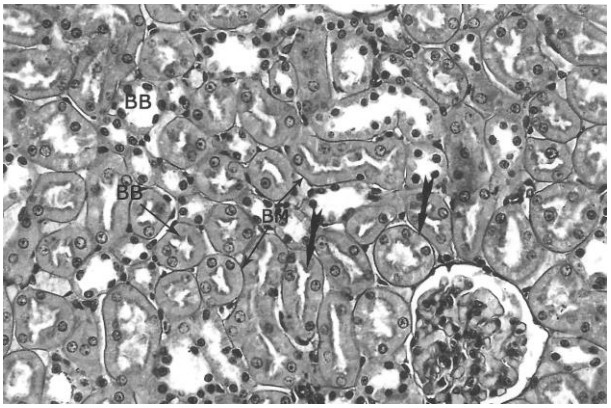

Figure No.1: Photomicrograph of microns thick PAS-H stained section from cortex of kidney in Group A (control) rat showing normal architecture of proximal tubules with intact Brush Borders (BB) and Basement Membranes (BM) X400.

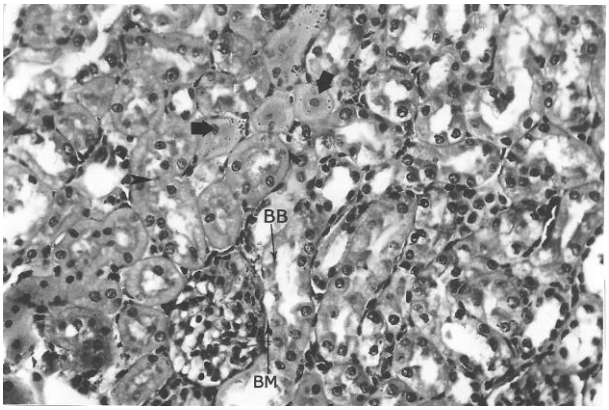

Figure No.2: Photomicrograph of 5 microns thick PAS-H stained section from cortex of kidney in STZ treated group B showing disturbed architecture with indistinct BB and BM, nuclear and epithelial debris in the lumina and tubules showing necrotic changes.x400.

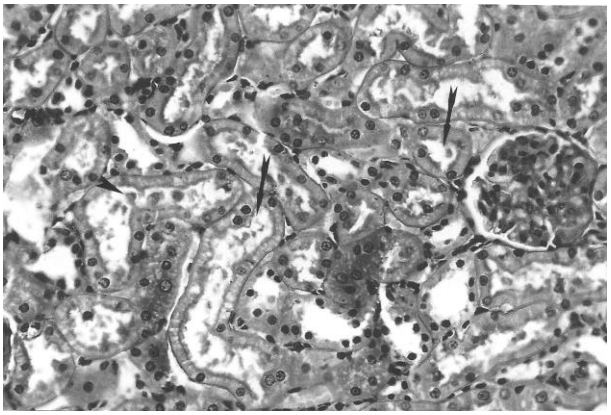

Figure No.3:PAS-H stained 5 micron thick longitudinal section of kidney from STZ and MEL treated group C showing dilated proximal tubules with epithelial casts in the lumina.x400.

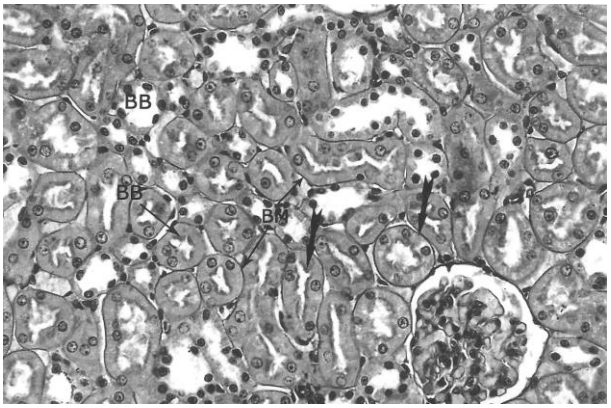

Figure No.4: Photomicrograph of 5 microns thick PAS-H stained section from cortex of kidney in Group D (MEL Treated) rat showing no change in proximal tubules with intact BB and BM.

DISCUSSION

The present study demonstrated the significance of MEL in reducing the severity of renal damage in animals exposed to a nephrotoxic drug like STZ. Since the kidney is highly susceptible to the toxic injury by a multitude of different drugs, it is not surprising that several antineoplastic agents may exert potent nephrotoxicity.STZ generates ROS which contributes to DNA fragmentation and evoke other deleterious changes in the cells[13].Petzold and Swenberg(1978)[14] demonstrated that a single I.V. dose of STZ induces strand breaks in kidneys and liver of rats.Alejandro D and Martha S(2002)[7] stated that STZ induces cell death by apoptosis and necrosis, which are in agreement to our results. Rodriguez et al in 2004 stated that oxidative stress and its constant companion inflammation play a major role in the pathogenesis of the progression of renal injury.MEL has potent antioxidant and anti-inflammatory properties and its production is impaired in chronic renal failure.

The favourable results seen with melatonin administration in our experiment are likely related to the antioxidant and anti-inflammatory properties of this compound resulting from its strong ROS scavenger properties.MEL has been shown to ameliorate inflammation by blocking transcriptional factors and tumour necrosis factor alpha[15] .In those situations where free radical production is enhanced, MEL has demonstrated to be more effective than other antioxidants with the advantage that lower doses are needed[10].It has been proved earlier that MEL could effectively neutralize the impaired anti oxidative status in rats with STZ induced diabetes.MEL has been shown to be effective in protecting against severe free radical mediated toxicity in a variety of conditions including chemotherapy[16], ischemia reperfusion injury[17] ,acute renal failure caused by mercuric chloride and gentamycin[18] In a study conducted by Naqvi A[12] in 1992, STZ at the dose of 37mg/kg for 6 weeks

produced marked hyperglycaemia in albino rats which is in agreement with our results. In the present study, STZ resulted in significant hyperglycaemia and MEL supplementation did not affect this parameter. In a similar study conducted by Sudnikovich et al in 2007[19], STZ administration to albino rats for 25 days resulted in significant hyperglycaemia, increased levels of glycated hemoglobin and retarded growth of animals, whereas melatonin administration did not effect these parameters.

Present experimental study reveals that the renal injury caused by STZ is not mainly due to hyperglycaemia, but due to its direct toxic effects on the morphology of the kidneys.M.Akmali in 2010[7] stated that STZ forms ROS which is responsible for its cytotoxicity. The present study further reveals that MEL preserves the morphology of the kidneys without producing a significant effect on blood glucose levels.

CONCLUSION

In conclusion, this study demonstrates that MEL administration suppresses the progression of renal injury induced by nephrotoxic drug like STZ.MEL could not decrease the hyperglycaemia in STZ treated animals, but it did prevent the histopathological damage of the proximal convoluted tubules caused by free radicals generated by STZ .So dietary supplementation of MEL could be an easy and inexpensive method of protecting cancer patients from renal damage caused by oxidative stress.

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Original Article

Frequency of Proteinuria in Patients with Older-Onset Diabetes Mellitus Attending Civil Hospital Karachi

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ABSTRACT

Objective: To determine the frequency of proteinuria in patients with adult-onset diabetes mellitus.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at Medical Wards of Civil Hospital Karachi from 1st November 2010 to 30th April 2011.
Materials and Methods: In this study 100 patients of adult onset diabetes mellitus were enrolled who were admitted in medical department at Civil Hospital Karachi. The duration of the study was 6 months. Diagnosed all patients with type 2 diabetes mellitus and > 40 years of age were included except for patients with urinary tract infection, haematuria, acute febrile illness, congestive cardiac failure, uncontrolled hypertension. A mid-stream urine sample was collected for the determination of UAE; Macroalbuminuria was tested first if it was found negative then urine was tested for Microalbuminuria.
Results: Out of 100 patients 55% patients had normal Albuminuria (<20 mg/liter) while 45% patients had evidence of increased proteinuria (>20 mg/liter). Out of 45 proteinuric patients, 28(62.2%) patients had evidence of Microalbuminuria (cutoff; 20-200 mg/liter) and 17(37.8%) patients had Macroalbuminuria (cutoff; >200 mg/liter)
Conclusion: The concluded that the frequency of microalbuminuria is higher than macroalbuminuria in type 2 diabetic subjects.
Key Words: Diabetes Mellitus, Microalbuminuria, Macroalbuminuria, Proteinuria, Diabetic Nephropathy

INTRODUCTION

Diabetes mellitus is a major global public health problem that is rapidly getting worse and projections of its future effect are alarming. According to the World Health Organization, diabetes mellitus affects 171 million people worldwide, and this number will rise to 366 million by 2030.[i] In Pakistan diabetes affects 5.2 million people and the number will rise to 13.8 million by 2030 [2].

Diabetic nephropathy is the leading cause of end stage renal disease and diabetes mellitus related morbidity and mortality and accounts for 30-35% of patients on renal replacement therapy [3-5]. Diabetic nephropathy is a clinical syndrome characterized by albuminuria on at least two occasions that are separated by 3-6 months. Diabetic nephropathy is defined as increased Urinary Albumin Excretion (UAE) in the absence of other renal diseases[5]. Diabetic nephropathy increases the risk of death, mainly from cardiovascular diseases[3,4].Diabetic nephropathy patients ultimately need haemodialysis and renal transplant and both of these are very expensive and hardly accessible especially in developing countries[3].

In diabetic nephropathy proteinuria is categorized into stages based on the values of Urinary Albumin Excretion (UAE); Microalbuminuria and Macroalbuminuria. Increased UAE is associated with increase in duration of diabetes, poor glycaemic control, decreased HDL-c levels, high blood pressure, dyslipidemia, genetic predisposition, smoking habits, age and male gender[3,4,6]. The diabetic nephropathy leads to End-stage renal disease and cardiovascular complications, therefore it is important to detect the nephropathy early and treat it accordingly. Thus the study will provide data of patients with proteinuria attending Civil Hospital Karachi so that the complications of diabetic nephropathy could be prevented.

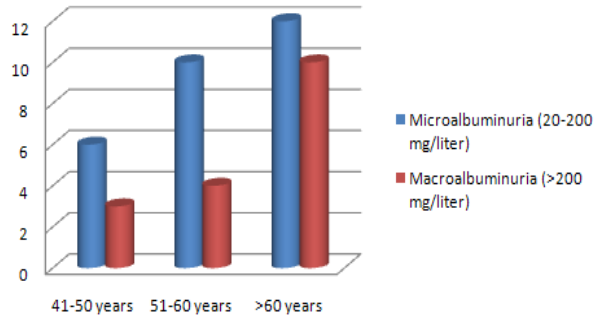
MATERIALS AND METHODS

This study was conducted at Medical wards of Civil Hospital Karachi from 1st November 2010 to 30th April 2011. This study consisted of 100 cases of diabetes mellitus admitted through the outpatient department, as well as from casualty department. Detailed history was taken from all the patients with special regard to bio-data, duration of disease, mode of treatment, history of hypertension, and complete physical examination including height, weight, body mass index (BMI), temperature and blood pressure. Inclusion criteria were that all the adults patients (Male and female) ,> 40years age of diabetes mellitus on the basis of history. Patients with urinary tract infection, haematuria, acute febrile illness, congestive cardiac failure, uncontrolled hypertension were excluded .

A mid-stream urine sample was collected for the determination of UAE; Microalbuminuria was tested by "Nephelometry Method (Beckmen Array 360 kit)"; while Macroalbuminuria by "Sulfosalicylic Acid Method of Albumin Determination". Blood samples were drawn for CBC, blood glucose levels, serum urea and creatinine levels and a chest x-ray P/A view was done assess the cardiac sizeData was analyzed through SPSS software.

RESULTS

A total of 100 patients with type 2 diabetes mellitus, above forty years of age, who fulfill the inclusion criteria, were included in this study. The average age of the patients was 55.93 ± 8.04 (95%CI; 54.34 to 57.52) Years. Out of 100 patients, there were 48% males and 52% females in this study with 1: 1.08 male to female ratio. Frequency of proteinuria according to age and gender are shown in Chart 1, 2.



Pearson Chi-Square = 1.13 DF= 2 P=0.56
Chart No.1: Proteinuria According to age.

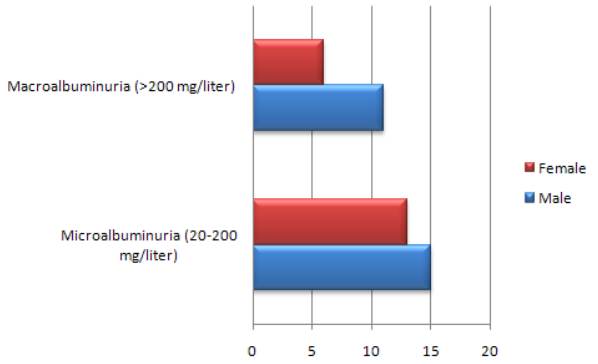


Chart No.2: Proteinuria According to Gender

In fifty-eight percent patients the duration of diabetes mellitus from the date of diagnosis was within ten years while in remaining 42% patients the duration of diabetes mellitus was more than ten years. Out of 100 patients 55% patients had normal Albuminuria (<20 mg/liter) while 45% patients had evidence of increased proteinuria (>20 mg/liter). Out of 45 proteinuric patients, 28(62.2%) patients had evidence of Microalbuminuria (cutoff; 20-200 mg/liter) and 17(37.8%) patients had Macroalbuminuria (cutoff; >200 mg/liter)

Out of 45 proteinuric patients, 20 patients were suffering from diabetes for less then ten years and 25 patients were having diabetes for more then ten years from the date of diagnosis.

DISCUSSION

Diabetic nephropathy is the leading cause of end-stage renal disease world wide and diabetes mellitus related morbidity & mortality and constitutes the major workload of dialysis centers[3]. Microalbuminuria is the first clinical evidence of kidney involvement and the process is potentially reversible at this microalbuminuric stage [3,4]. Microalbuminuria is also strongly associated with other cardiovascular risk factors and cardiovascular complications[7].

In our study out of hundred patients 55 patients (55%) were found to have normoalbuminuria while microalbuminuria and macroalbuminuria was present in 28(28%) and 17(17%) patients respectively. These study results are comparable with study conducted by Zeeshan[8] at Agha Khan University Hospital showing normoalbuminuria 58%, microalbuminuria 26% and macroalbuminuria 16%. While in other international studies prevalence of proteinuria was different. Rossi et al[9] showed microalbuminuria in 19.1% and macroalbuminuria in 3.5% patients. These differences in results in my and above studies are because of difference in sampling technique, various assays used for detection of microalbuminuria, control of diabetes, difference in inclusion criteria, difference in definition of albuminuria, life style modifications and different population studies etc.

In ourstudy out of forty-five proteinuric patients 26 were male and 19 were female. Male were slightly more affected than female but the proportion was not statistically significant (P value=0.46). However local study done by Rizwana Muzaffar et al [10] at Lahore showing no relation of gender with proteinuria. Another local study by Hashim et al[ii] also showed no association of gender with proteinuria. Age is considered one of the important factors affecting the development of proteinuria in diabetic patients; as the age progress the level of proteinuria also increase. In my study, no significant relationship was found between age and the development of proteinuria (P value=0.56). This correlates with the study done by Hashim et al [11].

Duration of disease in diabetics also affect the development of proteinuria. In my study it was observed that duration of diabetes mellitus has no effect on the frequency of proteinuria (P value=0.34). This study correlates with the local studies by Asma et al[12] at Bahawalpur, Hashim et al[11] at Lahore and Ghafoor F et al[13] who found no significant association between duration of diabetes and proteinuria.s

CONCLUSION

The frequency of microalbuminuria is higher than macroalbuminuria in type 2 diabetic subjects. All patients with microalbuminuria are prone to develop macroalbuminuria and hence overt nephropathy leading to end-stage renal failure and related cardiovascular complications. No significant association of age, gender and duration with the development of proteinuria was found in diabetic patients.

Recommendations:

All diabetics should be screened for microalbuminuria at the first presentation and then after every six months so if they found to have microalbuminuria in their urine, they should be subjected to appropriate treatment to retard the progression of nephropathy and associated complications.

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Original Article

Outcome of Low Dose Intralesional Steroid Injections in Superficial Infantile Capillary Hemangioma (SICH) of Eyelid

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ABSTRACT

Purpose: To evaluate the outcome of low dose intralesional steroid injections used in superficial infantile capillary hemangioma (SICH) of eye lid**.**

Study Design: Prospective Study

Place and Duration of Study: This study was conducted at Department of Ophthalmology, Chandka Medical College Hospital Larkana from September 2001 to October 2011.

Materials and Methods: Only, patients with congenital SICH involving eye lids with closure of visual axis were included in this study and SICH involving eye lids without closure of visual axis were excluded from study. The diagnosis of disease was based on history and clinical examination. All the patients were treated by mixture of low dose intralesional steroids triamcinolone 20mg (0.5ml) and dexamethasone 4mg (1.0ml). A total of three injections were given with interval of two months. After injection, the follow-up examinations were carried out at first week, every second month for six months and then annually. After treatment, outcome was recorded. The successful outcome was labeled when there was complete regression of lesion.

Results: Out of 37 patients 28(75.67%) were female and 9(24.32%) were male with female to male ratio of 3.1:1 and age range of 2 to 12 months. All the patients had unilateral growth; with left eye lid involvement in 22(59.45%) cases and right eye lid involvement in 15(40.54%) cases. The successful outcome seen was early regression of lesion in 24(64.86%) cases by age of 2.3 years and in 13(35.13%) cases by age of 3.1 years.

Conclusion: The outcome of this study was that, early treatment of SICH of eye lid with intralesional steroid injections resulted reliable, quick, beneficial effects and good cosmetically functional eye lid by early involution of growth.

Key Words: Intralesional Steroid Injections, Capillary Hemangioma, Anisometropia, Astigmatism, Amblyopia

INTRODUCTION

Hamartomas are congenital abnormal proliferations of normal tissue at normal site. The most common example of these is superficial infantile capillary hemangioma (SICH) of eye lid which is abnormal growth of vascular endothelial cells made up of masses of very small –caliber vessels.[1,2]. It is the most common benign soft tissue tumor of infancy. Approximately 4%-10% of children are suffering from these lesions in which half of these lesions involve the head and face with female: male ratio of 2.5-4:1.[3,4] Most of the lesions are not visible at birth but more than 50% of them are evident during 1-2months of early life and 90-100% in 6-8 months of life.[5] The lesion is diagnosed by history of red or purplish growth which becomes larger and thicker on crying of child. On inspection the lesion is strawberry in appearance and is non-pulsatile on palpation because of diminished blood flow. It empties with pressure and refills after releasing of pressure (empting-refilling sign).Indication of its treatment is threat of visual loss by occlusion, mass effect, amblyopia, and astigmatism.[6] Spontaneously most of the lesions involutes progressively in such a way that 40- 60% completely regressed by age 4 years and 76% by age of 7 years of life.[7]Treatment options are mixture of intralesional steroid injections-40 mg/ml triamcinolone + 6mg/ml betamethasone[8], oral steroids-prednisolone1-2-5mg/kg/day[9], topical steroids[10], interferon alfa-2a[11], vincristine[12], beta blockers[13], external beam irradiation[14], carbon dioxide laser , argon laser, Nd:YAG laser [15,16], pulsed dye laser [17], and surgical excision.[18]

MATERIALS AND METHODS

This prospective study was conducted from September 2001 to October 2011 at Department of Ophthalmology Chandka Medical College Hospital Larkana on 37 patients with unilateral SICH of eye lids. The patients were selected from the out-patient department after diagnosis of disease based on history and clinical examination of red or purplish growth increasing in size on crying of patient and strawberry, non-pulsatile in appearance with empting and refilling sign. All the patients were admitted in the eye ward where a specific proforma containing patient's bio-data, age, sex, laterality, site, treatment and their complications was filled. Only patients with SICH of eye lids with closure of visual axis were included tin this study and patients with SICH of smaller size not showing closure of visual

axis were excluded from study. To rule out systemic associations of SICH, complete blood cell count and ultrasound abdomen was performed in all cases. All the patients after aseptic measures received intralesional mixture of steroids injections triamcinolone 20mg (0.5ml) and dexamethasone 4mg (1.0ml). The eye lids were padded and patients were kept on oral antibiotic cephradine 30-50 mg/kg body weight/day and analgesic ibuprofen 15mg/kg body weight/day in divided doses for 5 days. Eye dressing was removed on the next day and topical antibiotic ointment was given for one week. The follow-up examination was carried out at first week, every second month for six months and then annually. After treatment outcome was recorded. The successful outcome was labeled when there was complete regression of lesion.

RESULTS

Our study included 37 patients, 28(75.67%) females and 9(24.32%) males with female: male ratio of 3.1:1 and age range from 2 to 12 months. The left eye lid was involved in 22(59.45%) cases and right eye lid in 15(40.54%) cases. All the patients were with unilateral growth causing complete closure of visual axis. With first local intralesion steroids injection in all cases, the immediate effects seen were violet discoloration and increase in size of growth followed by decrease in size of growth in 2-3 weeks. Due to insufficient decrease in size of growth and lid opening after two months of first injection, in all the patients further two doses of same mixture of intralesional steroid injections were repeated with interval two months in each injection. (Please see Annex). Outcome of injections was the early regression of lesion in 24(64.86%) cases by age of 2.3 years and in 13(35.13%) cases by age of 3.1 years.

Before Treatment **After Treatment**

Figure No.1: Color Photograph of 11 Months old baby girl with Superficial Infantile Capillary Hemangioma of the left upper eyelid before treatment and after treatment

DISCUSSION

Although SICHs of lid are benign in nature but when larger in size or sufficient to cause closure of visual axis and when these left untreated may lead to significant visual loss caused by anisometropia, astigmatism, amblyopia at early age and dysfunctional eye lid and cosmetic blemish later in life. Therefore they should be treated as earlier as possible at early age to prevent blindness and disfigurement. Study conducted by of Friedens IJ et al showed approximately 2/3 occurrence of SICH in females and 1/3 in males. The same was observed in our study with female to male ratio of 3.1:1.[3] Before starting treatment it is important to differentiate SICH of eye lid from dermoid cyst, vascular malformations (i.e.lymphangioma / arteriovenous malformations), metastatic neuro-blastoma, nevus flammeus (port-wine stain) and to search for systemic associations like high output heart failure (SICH with very large fast growing visceral hemangioma), Kasabach Merritt syndrome (SICH with thrombocytopenia, anemia, low levels of coagulating factors, large visceral tumors) and Maffuci syndrome (SICH with enchondromata of hands, feet and long bones as well as bowing of long bones).[19] Fortunately in our study we had not seen any of this case with systemic association. The synthetic topical, local intralesion and systemic steroids are widely used in various diseases of eyes involving lids, adnexa, anterior segment, posterior segment, cranial nerves related with eyes and disorders of many organ systems. Triamcinolone, dexamethasone are synthetic glucocorticoids steroids with marked anti-inflammatory actions like: Stabilizing cell lysozomal membrane which prevents release of lysozomal proteolytic enzymes; decreasing capillary permeability which prevents plasma loss and white blood cells migration into inflammed area; depressing white blood cells ability to digest phagocytized tissue which prevents further release of inflammatory materials; suppressing antibodies and T-cells which prevent immune reactions that cause inflammation; modifying the body's immune responses to diverse disease stimuli.[20,21,22] These corticosteroids can produce serious side effects like Cushing's habitus (a characteristic appearance with rounded face, narrow mouth, supraclavicular hump and truncal obesity with thin limbs, fragile skin, muscular weakness), susceptibility to infections, delayed wound healing ,peptic ulceration, osteoporosis, growth retardation, fetal abnormalities cleft palate, elevation of blood pressure and blood sugar, osteoporosis, psychosis, congestive cardiac failure and renal failure.[23] In our study we used intralesional mixture of triamcinolone 20 mg, which is long acting steroid and dexamethasone 4mg which is short acting steroid. During the follow up, the post injection, local intra-lesion complications seen were bleeding in 5(13.51%) cases, soft tissue atrophy in 4(10.81%) cases, hypo pigmentation in 3 (8.10%) cases and systemic hirsute in 2 cases (5.40%). Shorr N et al had noticed one of the most serious ocular complication, central retinal artery occlusion after use of mixture of local periocular intralesion steroids injection (40 mg/ml triamcinolone + 6mg/ml betamethasone), but contrast to this, in our

study we had not noticed such type of complication in any case, this may be due to use of low and divided doses of steroids 20 mg(0.5ml) triamcinolone with 4mg(1.0ml) dexamethasone.[8] Margileth AM et al noticed about 40% complete regression of lesion by age 4 years and about 70% complete regression by age 7 years without any treatment, but we observed early regression of lesion in 24(64.86%) cases by age of 2.3 years and in 13(35.13%) cases by age of 3.1 years with early treatment by local intralesion steroids injections.[7] In contrast to other expensive and unsafe methods of treatment for SICH, we noticed that local intralesion steroids injection treatment is not only cheap, easily approachable but results in early regression of lesion without significant local and systemic complications. Another important advantage of early regression of SICH of lid is to reduce the risk of refractive error, astigmatism, amblyopia, visual loss and cosmetic blemish. Hence we recommended that local intralesion steroids injections are important in controlling the growth phase, substantial shortening of the natural coarse and early regression of SICH. Although in our study family history was absent but patient's parent education about natural course of regression and genetic counseling is highly recommended.

CONCLUSION

We observed that early treatment of SICH with intralesional steroids results reliable, quick, beneficial effects and good cosmetically functional eye lid by early involution of growth.

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Original Article

Frequency of Hepatotoxicity Caused by ATT in Pulmonary Tuberculosis

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ABSTRACT

Introduction: Tuberculosis is common disease caused by Mycobacterium Tuberculosis. Tuberculosis is one of the world's most widespread and deadly illnesses and infects an estimated 20–43% of the world's population and kills about 3 million people each year in the world. The common side effect of antituberculous drugs is hepatotoxicity. This study was carried out to determine the magnitude of hepatotoxicity caused by antituberculous drugs in patients of pulmonary tuberculosis.

Objective: To determine the frequency of hepatotoxicity caused by ATT in pulmonary tuberculosis.

Outcome measure: Frequency of hepatotoxicity

Study design: Cross sectional study

Place and Duration of Study: This study was carried out in collaboration of Department of Medicine and Department of Pulmonology, Chandka Medical College, Civil Hospital Larkana from November 2010 to May 2011.

Subjects: All consecutive sputum smears or culture positive patients or radiological evidence of active pulmonary T.B of either sex, older than 15 years of age were included in the study.

Materials and Methods: After approval of ethical committee for medical research of Shaheed Mohtarma Benazir Bhutto University Larkana, informed written consent was taken from newly diagnosed patients of pulmonary tuberculosis for participation in the study. Blood samples were taken, coded and sent for determination of liver function test. Final outcome was measured at the end of 4th week. The data was analyzed using SPSS version 17.

Results: A total of 256 patients were enrolled in this study during study period. The mean age of enrolled participants is 41.5±18.1. Of 256 patients, 132 (51.6%) were male and 124 (48.4%) were female. The male to female ratio was 1.06:1. Mean serum bilirubin was 1.5±0.7 mg/dl (Range 1.1-3.9mg/dl), the mean alanine transferase level was 34.7±11 IU/L (Range 11- 109 IU/L), aspartate transferase level was 35.4±19.3 IU/L (Range 11-112 IU/L) and alkaline phosphatase level was 150±38 IU/L (Range 95-280 IU/L).The frequency of hepatotoxicity was 51 (19.9%). Hepatotoxicity was observed in 25-35 age group was 21.7% and 56-65 years was 26%. Hepatotoxicity was observed in 23.4% female and 16.7% male.

Conclusion: It is concluded from this study that patients taking anti tuberculosis therapy are vulnerable to hepatotoxicity. Screening should be done after starting of ATT in order to avoid liver damage.

Key Words: Anti-tuberculosis therapy, hepatotoxicity, liver enzymes, Chandka medical college.

INTRODUCTION

Tuberculosis is common disease caused by Mycobacterium Tuberculosis. Tuberculosis is considered to be most important communicable disease in the world in terms of Prevalence, morbidity, mortality and problems concerning its effective control. WHO declared the tuberculosis as a global emergency[1]. Tuberculosis is one of the world's most widespread and deadly illness and infects an estimated 20-43% of the world's population and killing 3 million people worldwide each year[2-3]. Someone in the world is newly infected with tuberculosis literally, with every tick of clock (one person per second)[4-5].

According to the World Health Organization's (WHO's) Global Tuberculosis Control 2009, Pakistan ranks eighth on the list of 22 high-burden tuberculosis (TB) countries in the world[6]. In 2007, an estimated 297,108 people in Pakistan (primarily adults in their productive years) developed TB. The case detection rate for Pakistan rose from 13 percent in 2002 to 67 percent in 2007, close to WHO's target of 70 percent[6]. The incidence and prevalence of all forms of tuberculosis in Pakistan is 181 and 223 per 100,000 persons per year respectively, and 29% of these die in a year[6]. The steep rise in case detection and the number of TB cases reported each year since 2000 is the result of nationwide efforts to increase involvement of private practitioners and community volunteers in identifying and referring TB suspects[6-7].

An effective control has been achieved by the widespread use of anti tuberculosis drugs. However, despite their efficacy, superadded problems have to be faced in terms of long duration of treatment, emergence of MDR strains and certain adverse effects ascribed to these drugs. Among these adverse effects hepatotoxicity is a well-known complication of Anti Tuberculosis Therapy (ATT) causing 19.7% cases[8-10]. The severity ranges from alteration in liver enzymes, chronic active hepatitis and picture of acute hepatitis, occasionally complicated by acute liver failure carrying very high mortality unless transplanted. It is common

with Isoniazid especially when given in combination with Rifampicin and Pyrazinamide. Ten to 20 percent of patients receiving Isoniazid as a single agent for prophylaxis against tuberculosis may have increased serum alanine and aspartate aminotransferase levels, but only 1 percent have hepatic necrosis severe enough to require the withdrawal of the drug[9-12]. Its incidence is reported to be lower i.e. 3-4% from developed countries as compared to 8-39% in the developing countries with the same regimens[13-16]. The clinical, biochemical and histopathological features of anti-tuberculosis induced hepatotoxicity are indistinguishable from that of viral hepatitis[17].

It has been postulated that hepatotoxicity induced by ATT is not truly idiosyncratic in essence. Rather certain genetic and environmental factors are attributed to coincide to produce sufficient quantity of toxic metabolites that then cause varied alterations in liver functions. ATT inducible cytochrome P-450 2E1 (cyp2E1) is constitutively expressed in the liver. Recent studies show that polymorphism of the N-acetyltransferase2 (NAT2) genes and glutathione-s transferases (GST) are the two major susceptibility risk factors for ATT induced hepatotoxicity[18-19].

MATERIALS AND METHODS

This is the cross sectional study, which was carried out in collaboration of Department of Medicine and Department of Pulmonology, Chandka Medical College, Civil Hospital Larkana. This study was done during November 2010 to May 2011. Sample size was calculated for population, proportion with specified absolute precision method. Assuming the anticipated prevalence of hepatotoxicity in tuberculosis patients in Pakistan at 19.6% (P), keeping the confidence interval (1-α) at 95% and absolute precision (d) set at 5%, the sample size is estimated to be as **256** patients by using WHO sample calculation software by above parameters.

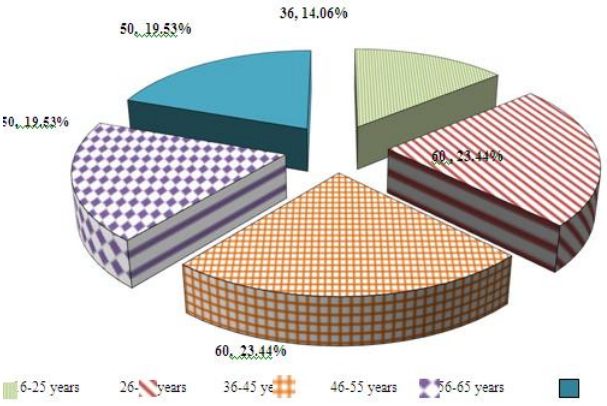
All consecutive sputum smears or culture positive patients or radiological evidence of active pulmonary T.B of either sex older than 15 years were included in study.

All patients above the age of 65 years with previous history of anti-tuberculosis therapy and evidence of chronic liver disease as viral hepatitis, alcoholic hepatitis, drugs and auto immune disorders were excluded from study. Patients suffering from chronic kidney disease, pregnant women and patients suffering from hemolytic disorders were also excluded from the study.

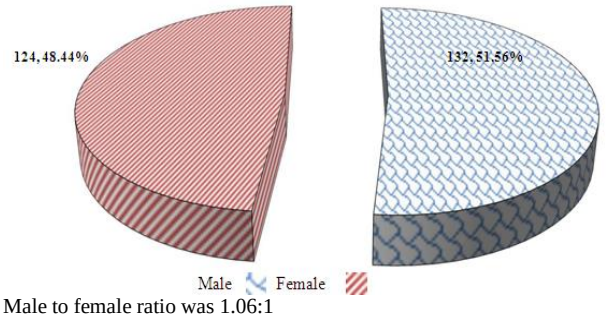
After approval of ethical committee for medical research of Shaheed Mohtarma Benazir Bhutto University Larkana, informed written consent was taken from newly diagnosed patients of pulmonary tuberculosis for participation in the study. Blood samples were taken, coded and sent for determination of liver function test (serum aspartate transferase "AST", serum alanine transferase "ALT", alkaline phosphatase "ALK" and serum Bilirubin) before starting anti-tuberculosis therapy and then weekly for first four weeks. Any patient who developed hepatotoxicity during course of therapy was evaluated to exclude other potential causes, such as viral hepatitis. Increased in serum amino transferases or alkaline phosphatase or serum bilirubin within 4 weeks of start of anti tuberculosis therapy, was labeled as positive for anti-tuberculosis therapy induced hepatotoxicity. Final outcome was measured at the end of 4th week. The data was collected and recorded to predesigned Proforma by the principle**.** The data was entered and analyzed using SPSS software version 17.0. Continuous variables as age, serum AST, serum ALT, serum ALK and serum Bilirubin was presented in mean ± SD (Standard Deviation). Categorical response variable as gender, age and presence or absence of hepatotoxicity was presented in frequencies and percentages for data presentation. Stratification was done with regard to age and sex to see effect of these variables on outcome.

RESULTS

A total of 256 patients were enrolled in this study during study period. The mean age of enrolled participants is 41.5±18.1 (Graph 1). Of 256 patients, 132 (51.6%) were male and 124 (48.4%) female. The male to female ratio was 1.06:1 (Graph 2). The descriptive of liver enzymes was summarized in table 1. Mean serum bilirubin was 1.5±0.7 mg/dl (Range 1.1-3.9 mg/dl), the mean alanine transferase level was 34.7±11 IU/L (Range 11-109 IU/L), aspartate transferase level was 35.4±19.3 IU/L (Range 11-112 IU/L) and alkaline phosphatase level was 150±38 IU/L (Range 95-280 IU/L).The frequency of hepatotoxicity was 51 (19.9%) (Graph 3). Stratified analysis based on age and sex was summarized in tables 2-3. Hepatotoxicity was observed in 25-35 age group was 21.7% and 56-65 years was 26%. Hepatotoxicity was observed in 23.4% female and 16.7% male.

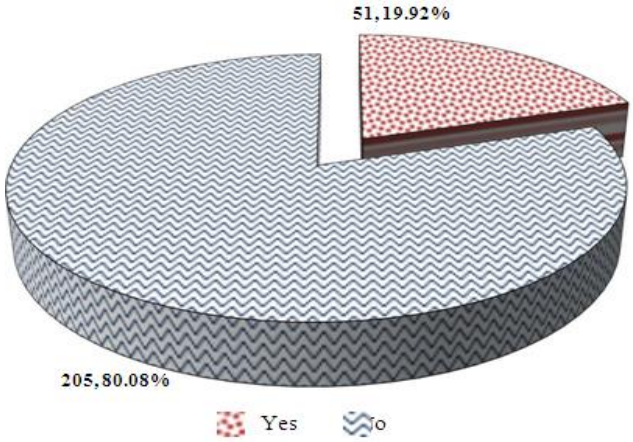


Graph No.1: Age distribution of enrolled participants (n=256)



Male to female ratio was 1.06:1

Graph No.2: Sex distribution of enrolled participants (n=256)



Graph No.3: Frequency of hepatotoxicity in enrolled participants (n=256)

Table 1: Descriptive of serum bilirubin and liver enzymes (n=256)

Variables	Means	SD	Range
Serum Bilirubin	1.5	0.7	(1.1-3.9 mg/dl)
Alanine Aminotransferase	34.7	11	(11-109 IU/L)
Aspartate Aminotransferase	35.4	19.3	(11-112 IU/L)
Alkaline phosphatase	150	38	(95-280 IU/L)

Table 2: Stratification of hepatotoxicity based on age

Hepatotoxicity	16-25 Years (n-36)	26-35 Years (n-60)	36-45 Years (n-60)	46-55 Years (n-50)	56-65 Years (n-50)	Total
Yes	19.4%	21.7%	11.7%	22%	26%	19.9%
No	80.6%	78.3%	88.3%	78%	74%	80.1%

Table No.3: Stratification of hepatotoxicity based on sex

Hepatotoxicity	Male (n-132)	Female (n-124)	Total
Yes	16.7%	23.4%	19.9%
No	83.3%	76.6%	80.1%

DISCUSSION

Tuberculosis constitutes major public health challenge, which is declared as global emergency by WHO[3]. Tuberculosis is a treatable endemic disease in Pakistan. Antituberculous therapy is the basic approach to control tuberculosis, but multiple antituberculous drug regimens exposing patients to liver damage[2,10]. Drug induced liver injury is a problem of increasing significance but has been a long-standing concern in the treatment of tuberculous infection. The liver has a central role in drug metabolism and detoxification and is consequently vulnerable to injury. The pathogenesis and type of drug induced liver injury are presented, ranging from hepatic adoption to hepatocellular injury. The knowledge of the metabolism of antituberculous medications and of the mechanism of hepatotoxicity is incomplete. Understanding of antituberculous drugs induced liver injury has been hampered by differences in study populations, definitions of hepatotoxicity, and monitoring and reporting practices[20]. In this study, the mean age of patients suffering from deranged liver enzymes was 41.5 years. This result was similar to mean age reported AKbri MZ[2], Yee D[12] i.e. 43.5 years and 40.3 years respectively, whereas vidal pla R[21], showed no specific relation with age. In this study female gender had got increased frequency of deranged liver enzymes, these results were comparable with Shakya R[10], Yee D[12] where as not comparable with Akbri MZ[2], Vidal pla R[21], where the gender had not influenced the results. In this study proportion of patients with deranged liver enzymes recorded 19.9%, while it was recorded as 40% by shakya R[10], 16.5% by vidal pla R[21], 16% by Akbri MZ[2] and 3% by Yee D[12], in their studies. The sample sizes were different in all these studies except Shakya R[10] that had studied patients those were comparable with our study.

In this study as well as in all other studies mentioned above, the therapy was continued despite the deranged liver enzymes. After two months in all studies patients with deranged liver enzymes had improved gradually.

None of the patients enrolled in our study, had deranged liver enzymes more than three times of the upper limit of normal level. This statement is also in agreement with all above mentioned studies.

There are few limitations in this study; first, this was a hospital based study not representative of population; second, in this study there was no comparative group. This study suggests that abnormalities of liver function are most likely to occur within the first eight weeks of treatment and during this period liver enzymes should be checked on four weekly bases, but monitoring the enzymes after this period should not be that much aggressive.

CONCLUSION

It is concluded that frequent monitoring of liver enzymes is essential to screen for the early liver damage due to antituberculous therapy. However mild increase in liver enzymes (less than three times of the upper limit of the normal level) doesn't warrant cessation of antituberculous therapy.

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Original Article

Indigenous Health Perception and Practices of the Punjab: An Anthropological Reflection

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ABSTRACT

Background: Anthropology is the most intimate humanistic explanation of human diversity as regards various small and large scales societies of the world. Anthropology aims to provide modern human civilization with understandable accounts of how human diversity that are not rooted in racial discrimination rather to bring us an opportunity to seek underlying rationalities and intellects associated with various historical, environmental, ecological, geographical, demographical, social, political and cultural compartmentalization and assortments.

Objective: To help health personnel to understand the local mind about the health and eudaemonia as perceived and practiced by the rural population.

Study Design: Observational (exploratory) study.

Place and Duration of Study: This study was conducted in the Union Council of Sacha Soda in the Tehsil and district of Sheikhupura district of the Punjab province from January 2011 to December 2011.

Materials and Methods: This study was based upon an intensive field works for three years in a Punjabi village Sacha Soda of Sheikhupura district on indigenous health paradigms. It is an anthropological reflection of an indigenous healthy dichotomy to which the researchers have termed "Sehat-Tandarusti" existing and prevailing in the rural Punjab.

Results: Punctuality in taking dinner (95.3%), washing hands before taking food (92.9%), mild walk after food (82.1%) and chewing sugar cane and maze as exercise of teeth (77.9%) were the most common good eating habits. Majority of the villagers were going into beds earlier (95%) and a high percent were getting up early (75%). Their first preference in case of illness was seeking help from Faith healers (86.1%) and the herbalists (88.9%).

Conclusion: There is a need to adopt the indigenous health perspective on *Sehat* (Eudaemonia) in order to promote the social awareness and effectively mobilize the populations towards better hygienic education and raising social responsibility among populations to contribute in making their livelihoods health friendly. The reinstating of the traditional health seeking system of practices can help the local populations to seek medical advices at local level as well as removing a threat from already overburdened urban health facilities

Key Words: Indigenous health practices, Medical anthropology, Traditional medicine.

INTRODUCTION

Medical Anthropology is a sub-discipline within Anthropology dealing with the Socio-Cultural attributes of Disease. It also studies the perception as well as practices related to various diseases and its peculiar curing practices within a particular society and its culture. Anthropology in its historical course focused upon the primitive societies to comprehend their socio-cultural system in order to negate the early and slanted sensing of primitive people as being 'savage' or 'uncivilized'. Rivers' work was among the earliest anthropological contribution on 'primitive medicine'. In his apprehension and extrapolation, he viewed primitive medicine as a social institution that is erected upon certain notions, underlying faith system as well as a colligation of inter-related curing practices that mostly comprised certain beliefs, ritual performances and practices well connected into the reasons of disease embracement and its anticipated indicators along with its therapeutic measures. The Routledge Encyclopedia of Social and Cultural Anthropology defines primitive medicine as: Primitive medicine' was seen as a coherent body of practices underpinned by particular ideas about the causation of disease that are, in turn, shaped by the general worldview of the members of that society.[1]

Primitive medicine as in modern terms 'Ethno-medicine', 'Traditional medicine' or 'Folk medicine' is now being recognized by the contemporary world. In this regard the observation made by World Health Organization is sufficient to grasp the importance and vitality of ethno-medical belief system and ethno-practices on various illnesses and diseases understood by modern health circles. WHO[2] comments on the health practices of the people in the current day world that: Although many populations in developing countries are reported as depending heavily on Traditional Medicine to help meet their health care needs, precise data are lacking. Quantitative research to ascertain levels of existing access (both financial and geographic), and qualitative research to clarify

constraints to extending such access, are called for. The focus should be on treatments for those diseases which represent the greatest burden for poor populations.

To understand the basic stance of paper, there is need to understand what is generally perceived as 'health' by Anthropology. Encyclopedia of Medical Anthropology defines Health as: "Health" as a broad construct, consisting of physical, psychological, and social well-being, including role functionality.[3]

Having considered the concept of 'health' inferred by Anthropology, the anthropological paradigm distinctly classifies difference between illness and disease. The Encyclopedia of Medical Anthropology further elaborates: Disease is something that is either cured, or not. But disease itself does not spur people to seek medical treatment; illness does. "Illness" is the culturally structured, personal experience of being unwell and it entails the experience of suffering.

Hahn[4] also crystallizes the stand point on the 'disease-illness' dichotomy. He expatiates on both of the concepts as disease is anchored in body whereas illness is a mental construction and is anchored in the mind. This interpretation examines that disease is a physically verifiable entity whereas illness is the entire concept of health concerned with well-being of an individual or a particular society. The belief system of a particular society comprises a connected notion of well-being in the realm of health. This difference between disease and illness invites Anthropologists to dig out the hidden social realities attached with the social construct of illness. The sub-discipline of Medical Anthropology thus helps researchers to interact with the local populations to study the native mind to thrash out the fabrics of the constructs of illness. This is especially done with regards to allowing medical anthropology to understand native mind-set and practices in order to improve the public health in countries and nations of third world.[5,6] Eisenberg[7] referred by Routledge Encyclopedia emphasizes that: Efforts to characterize non-biomedical views of ill health and approaches to its treatment in relation to the biomedical paradigm led to the development of the single most utilized analytic dichotomy in medical anthropology as a whole that of the disease/illness distinction (Eisenberg 1977).

MATERIALS AND METHODS

The current study was conducted in the Union Council of Sacha Soda in the Tehsil and district of Sheikhupura district of the Punjab province. Sheikhupura District lies roughly between North latitudes 31.0 degree and 32.5 degree and East longitudes 73.5 and 74.42 degree. Its shape is roughly that of trapezoid with a triangular off-shoot to the west from the Southwest corner. The village Sacha Soda is 18 km from Sheikhupura city towards North West. Data collection was done through the exploratory method while using main techniques of participant observation, in-depth interviews, and key informants. Participant Observation method helped in interacting with the village population in their natural life settings without making the respondents conscious about the study. This method was highly interactive and helped the team to build research rapport with the target population in their natural life setting. The most natural method of participant observation also helped in indicating the most relevant respondents (380 respondents) who were later on selected on random basis for in-depth interviews for more details about the local perceptions as well as practices. Key Informants were the gate to enter the field. These were local people from within the population having more detailed knowledge about the indigenous health's concept and the local cure remedies for specific diseases.

RESULTS

The village people usually observe this saying of prophet Mohammad (PBUH), "leaving the dinner doubles the speed of ageing" and also guide the youth to be punctual in taking the dinner. Similarly, after taking dinner the elders ask the youth to sleep without going for some other work so that the stomach effectively digests the food in-take.

Meat in-take should be appropriate in this regard a religious citation was quoted that meat eating should be at least once every forty days. In this regard, there was a myth about the meat eaters that they get into rage and are angry people.

Large quantity of liquids in-take is recommended by the elders of village in order to keep the pores of body smooth and producing perspiration, generally considered to be an indicator of good health. Drinking extremely cold water or any other form of liquid is prohibited. The justification for this habit is told that liquid channel of the body is hot and could create a freeze inside the body. Drinking liquids is said to be in sitting posture with a vessel of open mouth. The drinking habit is supported from a religious saying that holy Prophet (PBUH) desired all Muslims to sit while drinking water in three sips. This was also justified by the herbalist of village that in stomach there are fluids that help in digestion. Whereas, drinking in one go thins the liquids of the stomach that further create problems in digestion due to which bad stomach and digestion and pains are commonly reported.

Punctuality in taking dinner (95.3%), washing hands before taking food (92.9%) mild walk after food (82.1%) and chewing sugar cane and maze as exercise of teeth (77.9%) were the most common good eating habits. Large portion of food intake as vegetable, eating slowly, relax sitting posture, plenty of water intake were practiced by moderate percentage of the village people (around 60%). Avoiding extremely cold drinking water and standing while drinking was also practiced by vast majority. (table.1)

Table.1: Eating and drinking habits of the village people (n = 380)

Eating & drinking habits	No.	%
Punctuality in taking the dinner	362	95.3
Large portion of food in-take as vegetables instead of meat	247	65.0
Washing hands before taking breakfast, lunch or dinner	353	92.9
Eating slowly and maximum chewing of morsels	217	57.1
Relax sitting posture during eating	255	67.1
Eating while standing	11	2.9
Mild walk after food	312	82.1
Plenty of water intake	251	66.1
Drinking extremely cold water	10	2.6
Drinking water while standing	25	6.6
Chewing sugar cane and maize as the exercise of teeth	296	77.9

Getting early to the beds was common in the villagers because of their commitment in their fields. Earlier getting up in the morning was also a ritual among most of families to get ready for morning prayers and work in the fields or getting ready for schools or offices.

The elders also recommended that during sleep the pillow should be the one that is soft about five inches high from head for providing comfort to the neck and to avoid blood flow towards head during sleep.

Sleeping on right side was recommended by the elders under religious instructions of holy Prophet (PBUH). The justification given was that on left side of chest is heart which is busy all the day while cleaning the blood. During night, when people sleep, the heart also slows down its functions and in a way it also rest. Sleeping on right side is basically releasing body weight from the heart side. The elders also recommended avoid sleeping on left side or in an upright posture giving as a reason of bad dreams.

Table 2: Common practices of village people regarding their sleeping habits (n=380)

Sleeping habits	No.	%
Get in to the bed earlier	361	95.0
Earlier getting up	285	75.0
Use of soft pillow while sleeping	228	60.0
Pillow was said to be about five inches high from head	152	40.0
Sleeping on right side was recommended	331	87.1
Young males advised to drink one glass of water before sleep	300	78.9

Young males are advised to drink one glass of water before sleep to avoid the pre-mature ejaculation which according to local belief system brings physical weaknesses in the body.

Majority of the villigers were going into beds earlier (95%) and a high percent were getting up early (75%). High pillow was used by the low percentage and soft was preferred by majority (60%). Young males were mostly advised for a glass of water before going into bed (78.9%). Sleeping on the right side was a common practice. (table.2)

The people of the village, especially elders, were of the view that prevention is better than cure. Their first preference in case of illness was seeking help from Faith healers (86.1%) then the herbalists (88.9%). The moderate majority (66.1%), after failing cure by these two methods, was going to the local Homeopaths and 38.9% were going to the private practitioners for this purpose. (table.3)

Table.3: The practice of village people while seeking health consultation when sick (n=380)

Health consultation	No.	%
Prevention is better than cure	247	65.0
Home bound techniques	357	93.9
Faith healers	327	86.1
Herbalists	338	88.9
Homeopaths + Local GP	251	66.1
Medical facilities in urban centers	232	61.1
Private practitioner in a private hospital or clinic	148	38.9

DISCUSSION

The majority of village people clearly distinguish between Sehat and Tandarusti. Sehat as a concept to the villagers is not mere physical well-being rather it is more than that. It covers the overall living style that is deeply influenced by indigenous health perception out of which Islamic perspective remains a strongest part of this belief system. Villagers emphasize the preventive side of health care system to be the more than eighty percent important as regarded the curative aspect. The majority of the villagers believe in a commonly stated proverbial “Perhaiz Illaj Say Behtar Hai” (Precaution is better than cure). The people believe that their simple life pattern is best source of ensuring their Sehat as they opine that modern life and curses of technology especially the modern agricultural methods are now becoming a health and environmental hazards.[8]

According to local view (71 percent), the modern life style has put people in an unending race for material gains and physical comforts due to which mental stresses and strains have captured today’s man that are further making the earth an unhomely place. The struggle for material gains and getting more valuables

in life thus affects the Sehat of a man. The respondents' large majority believed that by revitalizing their indigenous life practices in terms of adopting simplicity can bring best scores regarding improvements in public Sehat.[9]

On the other hand, the modern methods in agriculture have raised the underground water pollution, loss in soil fertility, soil compaction, destruction of natural habitat for various wildlife forms as well as damaging the natural flora and fauna of the area. This phenomenon has further raised a visible decline in the health status of rural population.10 The local perception on Health consisted of two equal and complementary aspects of firstly, preventive and secondly curative side. The local population of the study area was found to be practicing both of these correlated aspects on health. The majority of the village community cites and thus practices the Islamic notion of hygiene.[11]

The respondents reported that preventive side of their medical beliefs and practices basically deals with the local concept of 'Sehat' (Eudaemonia). The village people believed that Islamic principles are based upon the principles of nature that can only ensure providing the best of 'Sehat' or health. In the following, the most common practices drilled by the 83 percent of the village population are mentioned. The traditional paradigm on Health according to the view of local community is the physical 'stoutness' and resistant immunity system.[12] The indigenous health perspective is erected upon the notion of 'curative aspect'. 87 percent of local community contacts the health personnel including the faith healers, herbalists, homeopaths and general health practitioners in case of contracting a disease. The approaching of specific health personnel depends upon various aspects depending upon the economic status of a particular family, age group, and gender of patient. The dominant majority of population believes that preventive side of health is more important in which balanced life style and hygienic practices help people avoid many health related issues and problems. As it is discussed in case of preventive aspects of health issues which enable people lead a simple and healthy life that ensures the stoutness of people.[13]

The mainstay of village is agriculture which is laborious profession that need physical and numerical strength therefore the hard work of agriculture related practices help people to maintain their physical and mental stoutness therefore they generally enjoy good physical wellness. The local health seeking behavior requires people to be cognizant of the individual preferences regarding curing and medication. This uniquely different behavior is reflected in day to day activities of people. The curing practices commence with the home made local practices including specific foods and herbal strategies and reinforcing them with the help of village herbalist or general practitioner. In case of psychological problems the village people (89 percent) are keen to consult the local faith healers who treat patients with the help of specific zikar (recitation) of Quranic words or verses. This set of practices includes the Taveez (amulets) in order to keep the effects of evil eyes permanently away from a patient especially a newly born infant or minors.

The local health seeking behavior starts from firstly home bound techniques; secondly, the consultations from village herbalist and faith healer; thirdly, the local homeopath or general practitioner; in case of failure in these three stages, comes the fourth stage of people seeking medical advice and cure from nearest medical facilities in urban centers. The fifth and last stage is the seeking of advice from a private practitioner in a private hospital or clinic.[14]

The local population describes its peculiar health seeking behavior with respect to their rural eco-systems that largely affect their local practices regarding health. The overall socio-economic environment of rural areas, existence of health department's infra-structure, easy approach of paramedical staff as well as the local cultural norms, belief system, and practices are closely interwoven.[15]

Ninety three percent of people in the village respond that once their livelihoods were sustainable in which they could easily take care of the health domain of the families but with the intensification and commercialization of their agricultural practices have put an incredible pressure over their meager economic assets due to which people after contracting a diseases usually prefer their homely and local practices. It is not generally the low preference given on health aspects rather it is the economic burden due to which they could not afford availing expensive health facilities available in the cities. The health facilities provided by the government in the village are not sufficient to meet the health needs of people at local levels. The rural health center usually portrays the scenes of ghost houses without presence of medical staff, doctors and acute dearth of medicines.[16]

CONCLUSION

To seek a health friendly environment for the nation, there is still much to do. At the same time, there is a need to adopt the indigenous health perspective on Sehat (Eudaemonia) in order to promote better health education in the country. This so because the indigenous perspective does not mean anything rooted in history rather it is the intellectual property of the local population developed and practices by people themselves. All there is an immense need to do is to revitalize the indigenous perspectives to make it according to the modern and current health standards of the nation. The indigenous perspective on Sehat can help promote the social awareness and can effectively mobilize the populations towards better hygienic

education and raising social responsibility among populations to contribute in making their livelihoods health friendly. The reinstating of the traditional health seeking system of practices broken due to current pressing economic pressure and burden can help the local populations to seek medical advices at local level as well as removing a threat from already overburdened urban health facilities. This step may also raise the self-sufficiency and self-reliance among the local population regarding health domain.

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Original Article

Placebo Controlled Study on the Efficacy and Safety of Calcipotriol in the Treatment of Mild to Moderate Psoriasis

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ABSTRACT

Background: Calcipotriol is a vitamin D analogue that has been used now a day as monotherapy in mild to moderate psoriasis. We have conducted a placebo-controlled clinical comparative study to assess the efficacy and safety of calcipotriol in the treatment of psoriasis.

Objective: To assess the efficacy and safety of calcipotriol in comparison with placebo in patients with mild to moderate psoriasis.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi from January 2008 to March 2008.

Materials and Methods: Sixty patients with mild to moderate psoriasis were enrolled after obtaining their informed written consent and were divided into two groups, A and B. Group-A was administered calcipotriol and Group-B was considered as placebo group for three months. The study parameter (Psoriasis Area and Severity Index, PASI) score was noted after every fifteen days (02 weeks) and were evaluated statistically at the end of the study period.

Results: The significant changes in mean ± SEM values were noted for the efficacy of calcipotriol during the period from day 0 to day 90 in group-A (calcipotriol) v/s group-B (placebo). According to the statistical evaluation, a reduction in the symptoms of the disease was found up to 67.8% in group A, and 0.5% in group-B. The difference between the results of both groups was noted to be highly significant ($P<0.001$).

Conclusion: Calcipotriol as monotherapy is observed to be significantly superior to placebo in terms of efficacy and safety in the treatment of psoriasis.

Key Words: Calcipotriol, placebo, psoriasis, psoriasis area & severity index.

INTRODUCTION

Psoriasis is a common, non-contagious skin disorder that causes rapid skin cell reproduction resulting in red, dry patches of thickened skin. The dry flakes and skin scales are thought to result from the rapid buildup of skin cells. Psoriasis commonly affects the skin of the elbows, knees, and scalp.[1] Psoriasis affects the life cycle of skin cells and causes cells to build up rapidly on the surface of the skin, forming thick silvery scales and itchy, dry, red patches that are some times painful.[2] Approximately 2-3% of the population worldwide is affected by psoriasis.[3] However, commonly accepted and validated diagnostic criteria are lacking. Psoriasis patients when compared to those with other dermatological disorders are among those who suffer from highest impact on their quality of life. Several lifestyle factors including alcohol and smoking have been associated with psoriasis. There is also evidence of association with other diseases including cancer. Psoriasis also accounts for considerable treatment costs, which should always be taken into consideration together with the relevant clinical outcome parameters.[4] Although the effect of psoriasis on a person's quality of life can be substantial, it is not well correlated with the extent of cutaneous involvement of the estimated 4.5 million adults in the United States who have psoriasis, about 450,000 indicate that at least 3% of their body surface area is currently involved, and only about 100,000 patients indicate at least 10% skin involvement. About 500,000 adults in the United States describe their psoriasis as being a substantial problem.[5]

Psoriasis is a skin condition that can take many forms. Most people live with just one of the types below, although there are rare cases in which a patient may experience more than one type. Plaque psoriasis is the most common type of psoriasis; nearly 90% of the people who live with psoriasis can have this skin lesion. Guttate psoriasis is the second most common type of the disease that accounts for up to 10% of people which usually affects people under age 30 years. Inverse psoriasis also called seborrheic psoriasis; this psoriasis

develops in skin folds such as the armpits, groins, under the breasts, around the genitals and buttocks. Pustular psoriasis, in which white blisters are commonly surrounded by red skin, is the hallmarks of pustular psoriasis. Erythrodermic psoriasis is the least common form of psoriasis that results in inflammation, itching, and a painful red rash that may peel and often covers the entire body. Psoriatic arthritis that affects up to 30% of people with psoriasis, which usually develops 5 to 10 years after the original diagnosis of psoriasis, although it can show up before a skin diagnosis.[6]

The primary cause of psoriasis remains unknown. Abnormal epidermal cell kinetics and abnormal activation of immune mechanisms are thought to be the major contributors and treatment may affect one or both of these mechanisms.[7] Calcipotriol is a vitamin D_3 analog, acts not only to inhibit cell proliferation and enhance cell differentiation in the skin of patients with psoriasis, but also appears to have effects on immunologic markers that are thought to play a role in the etiology of the disease. Calcipotriol ointment 50 micrograms/gm twice daily provided similar or superior efficacy to several other anti-psoriatic agents in adult patients with mild to moderate psoriasis.[8]

This study evaluated the role of calcipotriol alone v/s placebo in treatment of psoriasis and to verify efficacy and safety of calcipotriol.

MATERIAL AND METHODS

This study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre (JPMC), Karachi. The patients were selected from Department of Dermatology JPMC, Karachi during the period from January to March 2008. A total of 60 patients were enrolled in this study after taking their written consent to complete the full course of therapy and were divided into two equal groups named group-A and group-B.

Inclusion Criteria:

- Patients with mild to moderate psoriasis.
- Patients of either sex (male or female)
- Age 18 years or above.
- Patients suffering from psoriasis with percentage of Body Surface Area (BSA) affected by psoriasis $\leq 10\%$.

Exclusion Criteria:

- Patients suffering from hepatic or renal diseases.
- Pregnant or lactating women.
- Patients under treatment with retinoids or antibiotics.
- Patients with other skin diseases.
- Any other chronic ailment requiring prolonged treatment.
- Allergy to study medication.

We have used calcipotriol ointment 50 micrograms/gm twice daily in group-A patients and severity of the disease was assessed by Psoriasis Area and Severity Index (PASI). The severity of psoriasis has traditionally been evaluated by objective measurement of the extent of the body surface affected and consideration of the subtype of psoriasis, degree of disability and feasibility of topical therapy. The Psoriasis Area and Severity Index (PASI) score can be used as such a measurement of psoriasis severity. It includes the amount of body surface area affected by psoriasis in addition to three major symptoms i.e., redness, inflammation and scaliness of the skin lesion.[9]

Study Design: A total number of 60 patients of either sex were enrolled and divided into two groups, each group having 30 patients, designated as group-A (calcipotriol ointment alone), while in group-B we had used ointment base only. All the values were taken as mean ± SEM. The primary efficacy measurement was the mean change in (PASI) score from baseline to the endpoint i.e., at day 90. In our study, there were many quantitative variables therefore; we had applied chi-square. Student t-test was used to analyze the data at P value 0.05 for statistical significance.

RESULTS

Our final analysis included 60 patients, who had completed the whole study period. The age, sex, marital status and family history was recorded and as shown in Table-1. In group-A, a total of 30(50%) patients were studied, in which 18(60%) were male & 12(40%) were female, mean age was 33.5 years, range 18.5 years, in which 18(66.6%) had positive family history of psoriasis and 9(33.3%) patients had no family history of such disease. In group-B, a total of 30(50%) patients were studied having 17(56.6%) were male and 13(43.3%) were female, the mean age was 32.5 years, range 18.5 years, among those 16(64%) patients had positive family history of psoriasis and 9(36.3%) had no family history of such disease.

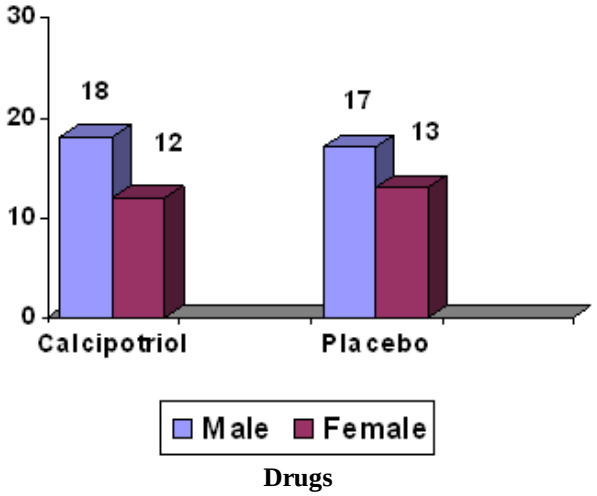

Figure No.1: Gender Distribution of Study Subjects

Table No.1: Demographic, Social & Professional Variables of Patients

Total study subjects (n=60)	Calcipotriol group (n=30) (%)	Placebo group (n=30) (%)		*P*-value*
Male	60.0%	Male	56.6%	<0.05
Female	40.0%	Female	43.3 %	<0.05
Age 20-39 (yrs)	31.6 ± 0.4	Age 20-39	31.60 ± 0.4	-
Age 40-60 (yrs)	51.8 ±0.5	Age 40-60	51.80 ±0.5	-
Educated	33.3 %	Educated	33.3 %	<0.05
Uneducated	66.6 %	Uneducated	66.6 %	<0.05
Laborers	66.6 %	Laborers	66.6 %	<0.05
Farmers	16.6 %	Farmers	16.6 %	<0.05
Drivers	13.3 %	Drivers	13.3 %	<0.05
Extra works	3.3 %	Extra works	3.3 %	<0.05
Married	66.6 %	Married	66.6 %	<0.05
Un-married	33.3 %	Unmarried	33.3 %	<0.05

The basic demographic variables shown in percentages and chi-square of association were applied for significance.

Table No.2: The Efficacy of Calcipotriol in Mild to Moderate Psoriasis

Improvement after calcipotriol treatment in weeks	*t* test	Mean Difference	*P*-value	95% Confidence Interval	
				Lower	Upper
WEEK-1	4.8	4.0	0.003	2.0	6.0
WEEK-3	5.7	5.5	0.000	3.3	7.6
WEEK-6	6.4	7.0	0.000	4.6	9.3
WEEK-9	6.0	6.0	0.000	3.7	8.2
WEEK-12	5.4	5.0	0.001	2.8	7.1

DISCUSSION

This present study demonstrates statistically significant changes in both groups in the parameter of PASI. In group-A, we applied calcipotriol local application once daily and observed a reduction of 67.89% in PASI at the end of study ($p<0.001$).

Our study match with the study of Austad et al (1997)[10], who conducted two parallel trials of 6 and 8 weeks and observed a reduction of 58.7% and 50.9% which are nearer to our results. The improvement in the parameter of PASI seen during the period of Day 0-90 and in group-A (calcipotriol) 15.5±8.8 pre-treatment after three months 14.00±7.937 were improved, p-value <0.05 and results were highly significant in our study. In case of safety of calcipotriol 3.00 ±1.5, p value >0.317 results were insignificant. The results of our study are also matching with results of Schwartzel et al (1996)[11] who conducted two trials comparing twice daily and once daily regimens of calcipotriol in 480 patients, the efficacy wise percentage change in PASI scores and observed a more than 60% reduction in once daily regimen i.e., in accordance to our study.

Lebwohl and colleagues (1998)[12] evaluated the use of calcipotriol and corticosteroids for the treatment of mild to moderate psoriasis and after two weeks of daily combination therapy 40 subjects (out of 44 demonstrated, 50% are greater improvement in Psoriasis Area and Severity Index (PASI) at the end of 6 months treatment, 76% of subjects shown remission. The researcher in this study also found the calcipotriol in combination was tolerable to the patients and that this combination improved remission, rates in the 2nd phase of sequential therapy. In our study about 67.3% reduction seen in PASI, scores and no patients in this group complained about itching or irritation. These results and observations are seen in accordance with the study of Lebwohl and colleagues. But in our study calcipotriol had improved 67.89% as compared placebo in the treatment of psoriasis. The improvement in the parameter of PASI seen during the period of Day 0-90 and in group-A (calcipotriol) 15.5±8.8 pre-treatment after three months 14.00±7.937 were improved, p-value <0.05 and results were highly significant in our study. In case of safety of calcipotriol 3.00 ±1.5, p-value >0.317 results were insignificant.

A review of medical literature from 1996 to 2002 was conducted using guidelines set by QUORUM statement criteria. In monotherapy studies, corticosteroids caused fewer adverse drug reactions compared to vitamin D analogues and tazarotene. Irritant contact dermatitis was the main side effect seen with vitamin D analogues.[8]

Calcipotriol is a synthetic analog of vitamin D_3 that inhibits keratinocyte proliferation and induces terminal differentiation. Calcipotriol is effective for psoriasis and a few studies have reported efficacy in nail psoriasis. This study shows the efficacy of calcipotriol in 24 patients with nail psoriasis. In this study, 14 patients showed significant clinical improvement after 3 months of therapy, and two of them became completely lesion-free after another 2 months. Topical calcipotriol is an effective treatment for nail psoriasis; its high tolerability allows its prolonged usage without severe side effects. Therefore, it can be considered to be a safe topical treatment in chronic cases.[13] According to the study of thaci et al[14] calcipotriol solution is an effective, safe, well-tolerated and cosmetically acceptable treatment modality. He found that this treatment was found to be a valuable supplement to previously available and established treatments for scalp psoriasis

CONCLUSION

Calcipotriol as monotherapy is observed to be significantly superior to placebo in terms of efficacy and safety in the treatment of psoriasis.

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Original Article

Incidence of Anemia in Pregnancy. A Randomized Study at PMC Hospital Nawabshah

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ABSTRACT

Background: In this part of the world anemia is one of the major public health problems especially in pregnant women. In our country the most important cause of anemia is poor diet repeated pregnancies and lack of awareness about contraception. Anemia can easily be managed with well nourish diet, with supplements of iron folic acid and multivitamin tablets. In our areas socio-economic problem is one of the causes which can be cope with help of Government and Non- Governmental Organizations by providing iron tablets and iron fortified foods to the population as a prophylaxis. To improve their health, pregnant women should regularly visit the clinics of Obs & Gynae and follow instructions of attending doctors and practice birth spacing in between the pregnancies.

Object: To determine the incidence of anemia in pregnant women in different socioeconomic classes in rural areas.

Study Design: Cross-sectional observational study.

Place and Duration of Study: This study was conducted at the Department of Gynae & Obs, Peoples Medical College Nawabshah, and Sindh Pakistan from 1st March 2009to 30th June 2009.

Patients and Methods: 850 pregnant ladies were included in the study who came to attend the antenatal clinic; where their history and clinical examination were recorded on a Performa. The ladies were divided into three socioeconomic classes, the higher, middle and lower class. 3ml of blood sample was taken from all the ladies for hemoglobin estimation and other necessary Lab test

Results: A total number of 850 participants were included in this study, out of those 329 pregnant women were having hemoglobin (Hb) below 9 gm/dl, declared as anemic, the incidence as observed was 38.77 % and the highest incidence was found in lower socioeconomic class.

Conclusion: It can be concluded from this study that anemia is one of the major problem in pregnant women of rural areas. The incidence observed was 38.77% which was least (0.6%) in higher class and was highest (60.2%) in lower socioeconomic class.

Key Words: Anemia, Pregnancy. Socioeconomic Classes, Hemoglobin Estimation.

INTRODUCTION

Anemia of pregnancy directly or indirectly contributes to a significant proportion of maternal death, according to the world health organization. The prevalence of anemia in women indicates that about half of pregnant women in the world suffer from nutritional anemia [1]. There are marked physiological changes in the composition of the blood in healthy pregnant women mainly to combat risk of hemorrhage at delivery plasma volume & red cell mass increase by 50% and 18.25% respectively, resulting in dilution of blood, decrease in Hb concentration called physiological anemia of pregnancy [2]. Anemia of pregnancy is often of multiple etiologies Iron and folic acid deficiency are the most important etiological factors. Malaria and worm infestation are other cause of anemia. Anemia is a common complication of pregnancy during which developing fetus may deplete the maternal iron stores [3] severe anemia can lead to cardiac failure in pregnancy, while lesser degree of severity are associated with maternal morbidity like hemorrhage infection and poor healing wound. It also contributes to prenatal morbidity and mortality by increasing the risk of intrauterine growth restriction and premature delivery'[4]. Anemia is public health problem worldwide. Anemia can be caused by innumerable factors, the most common being deficiency of essential elements for hemoglobin synthesis (i.e. Iron, Vitamin B12 and folic acid), blood loss, repeated pregnancies in female of reproductive age, worm infestation. hemolysis due to known or unknown causes and bone marrow conditions causing suppression of red blood cell synthesis. Chronic ailments like chronic renal failure, rheumatoid arthritis and tuberculosis are also known causes. In elderly female genital blood loss due to pelvic malignancies and in both sexes gastrointestinal blood loss is an important cause of anemia[5,6].

Globally, the most common cause of anemia is believed to be the iron deficiency due to inadequate dietary iron intake, physiologic demands of pregnancy and rapid growth and iron losses due to parasitic infestation[7]. Iron deficiency anemia is still a major nutritional and public health problem in developing countries including Pakistan it is estimated that 50'% of pregnant women in developing countries and up to 80% in South Asia have iron deficiency. Menstruating women present a large healthy population in which iron deficiency anemia

(IDA) is common, occurring in 5 — 10%. Menstrual loss, especially menorrhagia, pregnancy and breast feeding are usually responsible for anemia[8].

PATIENTS AND METHODS

The study was conducted in Gynae & Obs out Patient Department of PMC Hospital Nawabshah. This study was performed on 850 pregnant women of age ranging between 18- 40 years and having gestational age between 8 wks to 40 wks (Table-1). History and clinical examination was carried from all patients. Performa which include Name, age, occupation, address, gestational age, Hb estimation and prescribed treatment are to be filled. 3ml of blood samples taken for Hb% estimation and for other Lab tests. A cut of value of < 9.Ogm/dl of hemoglobin was used to define anemia.

Inclusion Criteria: All those pregnant women at their regular antenatal checkup.

Exclusion Criteria: Those pregnant women, having any co-morbidity like heart disease, liver disease. Thalassemia & hemolytic anemia were excluded from this study.

RESULTS

In the current study, a comprehensive scheme for collection and compilation of data was adopted by selecting a systematic random sampling of 850 pregnant ladies. Total number of 850 cases were included in the study; out of which 329 patient were detected as anemic having hemoglobin level below 9.0 gm/dl, the incidence is 3 8.77%, which is lowest in high socioeconomic class and highest in lower socioeconomic class as shown in the table-2.

Table No.1: Demographic Data

Number of cases	850
Age (years)	18-40
Mean age (years)	28
Gastational Age (weeks)	8-40

Table No.2: Cases of anemia according to different socioeconomic classes (n-329)

Socioeconomic Class	No of Cases	Hemoglobin Level			
		8-9 gm/dl	7-8 gm/dl	6-7 gm/dl	< 6.0 gm/dl
High	02 (0.6%)	02	--	--	--
Middle	129 (39.2%)	63	34	28	04
Low	198 (60.2%)	78	56	38	26
Total	329	143	90	66	30

DISCUSSION

Iron deficiency is generally recognized as the most common nutritional deficiency worldwide[9]. Nutritional anemia is a condition in which the hemoglobin content of the blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency[10.] Nutritional iron deficiency is highest in population segments that are at peak rates of growth. namely infants, young children and pregnant women. Pregnancy is a time in which the risk for developing iron deficiency anemia is highest. because iron requirement are substantially greater than average absorbable iron intake. Anemia is considered one of the main nutritional deficiency disorders affecting a large fraction of the population not only in developing but also in developed countries. Poverty, gender bias and lack of education about the importance of intake of balanced and iron-rich diet contribute to it[11]. In pregnant women nutritional anemia is often a serious refractory problem. It has been associated with a range of adverse consequences including poor mental development. reduced productivity, maternal mortality, and low birth weight. Iron deficiency is considered the main cause of anemia, especially among young children and pregnant women, who are at increased risk due to their increased requirements. Iron deficiency anemia has been eliminated from the developed world due to improved antenatal care and prophylactic iron therapy. It confirms to be a major problem in anemia of child bearing age in the developing world. The hemoglobin concentration hematocrit and red cells mass fall during pregnancy because expansion of plasma volumes is greater than that of red cell mass. The lowest normal Hb% level in non pregnant women is I 2gm/dI. The Hb% level in pregnant women is 11 .O gm/dI which acceptable to the world health organization'.

Incidence of anemia range from *35* to 90% among the pregnant women[12]. The estimated prevalence of anemia in middle income patient is 20 to *30%* whereas the corresponding figure among pregnant in lower income group is 60 to 70%. The main etiological factor of anemia may include poor nutrition, increase demand or loss. repeated pregnancies and lack of contraception[13] . In current study anemia was present in only 0.6% of cases in high socioeconomic class, 39.2% in middle class & 60.2% in lower socioeconomic class, such difference may be due to poor diet repeated pregnancies and lack of contraception. Anemia in pregnancy is an important preventable cause of maternal and parental morbidity; mortality. Anemia is a condition of low circulating hemoglobin in which the HB concentration has fallen below a threshold lying at two standard deviations below the median of a healthy population of the same, age, sex and stage of pregnancy[14]. The overall prevalence of anemia is estimated to be about 40% of the world population. The prevalence is 35% for non-pregnant women and *51%* for pregnant women globally, and tend to be 3 to 4 times higher in non-industrialized than in industrialized countries. Anemia affect about I 8% of women during pregnancy while in

non-industrialized countries prevalence varies between 35-*75°/s* with the average being 56%. The incidence is very high in Central Asia it may reach up to 8O%. The situation is particularly severe in Asia where three quarters pregnant women are anemic. The incidence of anemia varies in certain countries 49% in Bangladesh and 84% in Uganda. In Gilgut prevalent ratio is 43.17%. Routine antenatal care service provide particularly during second and third trimester of pregnancy when the demand of iron increase for the mother & developing fetus. Pregnant women are particularly vulnerable to anemia due to increase iron demand of pregnancy.[15]

Pregnancy heightens iron needs to accommodate the 40% increase in blood volume, and to supply the iron demands required for the growth of the fetus, placenta, and other maternal tissues. Iron absorption increases during pregnancy, although the majority of women are still unable to meet their iron needs without supplementation especially during the 2nd trimester of pregnancy [16&17]. During the second trimester. iron requirements begin to increase and continue to do so throughout the remainder of pregnancy. The increase in oxygen consumption of both mother and fetus is associated with major hematologic changes. During pregnancy. the fetal demand for iron increases maternal daily iron requirements from < I to *2.5* mg/d in early pregnancy and 6.5 mg/d in the third trimester[18]

CONCLUSION

It can be concluded from this study that anemia is one of the major problem in pregnant women of rural areas. The incidence observed was 38.77% which was least (0.6%) in higher class and was highest (60.2%) in lower socioeconomic class which may be due to poor nutrition, increase demand or loss. repeated pregnancies and lack of contraception in this class.

Recommendations:

Anemia can fairly be managed with diet, iron folic acid, multivitamin and good family planning education. In our areas socio-economic problem is one of the causes which can partly be managed with the addition of prophylaxis, iron supplement free of cost in public general hospital and iron fortified foods to the population[19]. So for improving the condition of pregnant women they regularly visit the OPD & follow their instruction and birth spacing in between the pregnancies.

A recent critical review of the scientific evidence indicated that the biological effect of iron deficiency anemia on work capacity is sufficiently strong to justify improving iron status among adult women[20]. Iron supplementation is one of the recommended strategies to improve iron status in the vulnerable groups. Several forms of iron salt are used to treat iron deficiency remarkably; however, the treatment used by the 19th century's French physician Blaud (ferrous sulfate) is still as effective as any other oral therapy.

The WHO recommends large-scale programs of daily iron supplementation to reduce the prevalence of anemia in high risk areas·. The center for disease control and prevention and the American College of Obstetricians and Gynecologists recommend a daily iron supplement (30mg) as prophylaxis for iron deficiency during pregnancy.

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Original Article

Frequency of Hepatitis-D in HbsAg Positive Cases at Peoples University of Medical & Health Sciences for Women Hospital Nawabshah

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ABSTRACT

Objective: To find out the frequency of delta virus (HDV) in HBV positive patients
Study Design: Observational Study
Place and Duration of study: This study was conducted at the Department of Medicine PUMHS Nawabshah form 01-01-2011 to 31-12-2011.
Materials and Methods: 200 adult patents of conformed Hepatitis B were included in the study blood samples of all the patients were screened for HDV by Elisa method / PCR during period of one yare.
Clinical status of positive and negative patients was also compared.
Results: Anti HDV was found in 32 patients (15%1) among them 20 (62%) were male and 12 (38%) were female.
Conclusion: The prevalence of HDV infection in HBV +ve patients is significant our area.
Primary eradication of Hepatitis B virus is required
Key Words: Hepatitis D virus, in chronic Hepatitis B Sindh.

INTRODUCTION

Hepatitis D virus (HDV) is a defective RNA virus that depends on the hepatitis B surface antigen (HBsAg) of hepatitis B virus for its replication, developing exclusively in patients with acute or chronic hepatitis B[1]. Simultaneous infection with HDV tends to accelerate the progression of chronic hepatitis B virus (HBV) to chronic active hepatitis, cirrhosis, and hepatocellular carcinoma and mediates fulminant hepatitis. Approximately 5% of patients with chronic hepatitis B infection worldwide are infected with hepatitis D virus. Its prevalence in Italy, eastern Europe, and western Asia is higher than in the rest of the world, reaching 83.3%, 8.3%, and 12.5% in Romania, Italy, and Russia, respectively[2,3].

A recently published large sample size study demonstrated in Pakistan seropositivity of HDV infection in 16.6% and disease is more common in central part of country[4]. This virus can not live or replicate unless with the envelop of Hepatitis B-Virus and similar to healthy carriers of hepatitis B[5]. It is estimated that 5% of hepatitis B surface antigen (HbsAg) positive carriers are infected with HDV[6]. It is known that coexistent infection with HDV tends to accelerate the progress of chronic HBV infection to chronic Hepatitis, cirrhosis and hepatocellular carcinoma[7]. Hepatitis Delta virus (HDV) and Hepatitis B virus (HBV) co-infection is well known to induce a spectrum of acute and chronic liver diseases which further advance to cirrhosis, fulminant hepatitis and hepatocellular carcinoma (HCC)[8]. In Africa, the Middle East and southern Italy, up to 24% of carriers of Hepatitis B virus surface antigen (HBsAg) have markers for HDV. Conversely, infection with HDV is uncommon in the United States[9].

My rational is the determine the frequency of delta virus infection in hepatitis B+ve cases in the local population report at Peoples university of Medical and Health Sciences Nawabshah.

MATERIALS AND METHODS

This study was conducted at Medical Department of Peoples University of Medical & Health Sciences for Women Hospital Nawabshah during the one year period from 01-01-2011 to 31-12-2011. 200 patients aged between 15-60 years of both sexes, males 124 (62%) & 76 (38%) females, were confirmed cases of Hepatitis B by Elisa & PCR were screened for HDV-anti bodies, after informed consent, and were included in the study. Patients below 15 years, HCV +ve patients, in malignancy & Patients on Dialysis were not included in the study. This is an observational study,

Patients fulfilling the inclusion criteria were admitted in Medical Unit-I of PUHMS,Hospital Nawabshah. After taking detailed history and doing clinical examination, were subjected to relevant investigations i-e blood anti HDV antibodies on Elisa and PCR.

Other important investigations like HBeAg, Anti HBe antibodies, HBV-DNA, Serum ALT, S. Albumin & Haemoglobin level of each Patients were also carried out.

After collection of data analysis and comparison between anti,HDV+ve and Anti HDV –ve (all HBsAg+ve) was made.

It was conducted by using statical package for social Science (SPSS) software Version 16.

Effect modifier like Gender & age was controlled by stratification.

RESULTS

A total of 200 patients with HBsAg+ve were observed over a period of 12 months. From 01-01-2011 to 31-12-2011 the demographic characters are presented in table 1. There were 124 (62%) Male Patients & 76 (38%) females. Age limit was 15-60yaer – more were between 20-40 year of age.

Majority of the patients were married & belong to rural area Sind. The male patients were younger than females Hbs Ag was +ve in all patients by Elisa /PCR.

HDV RNA was detected in 25 patients: (12.1%). Anti HDV antibodies were positive in 32 Patients (15.1%)

20 males (62%) And 12 (38%) females. Among anti HDV +ve Patients anti HBe was present in 20 Patients (62%).

In anti HDV Negative patients it was dected in 35 (20.83) patients (P=0.30). HBeAg, marker of active replication of HBV was+ve in 80 (45%) HDV positive patients while it was negative in 60 (59.75) patients.

Table No.1: Clinical characteristic of 200 study patients

Variable	Number	Percentage (%)
Male	124	62
Female	76	38
Rural	150	75
HBeAg (reactive)	80	45
Anti-HBe	20	62
Anti-HDV	32	15.1
HDV-RNA (Detected)	25	12.1
Hepatomegaly	62	13.1

Table No.2: Comparison between Anti-HDV positive and Anti-HDV negative Groups.

Variable	Anti-HDV Positive(n=50). No.(%)	Anti-HDV Negative (n=50). No. (%)
Gender Male Female	 20 (62.) 12 (38)	 104 (80) 64 (88)
HBeAG (Reactive)	80 (45)	60 (59.75)
Anti-HBe	32 (15.1)	168 (84.9)
Age (in years)	32±50	20±30
Serum ALT (IU/L)	70±95	50±60
Serum Albumin (g/dl)	2.5±0.5	2.81±0.61
Haemoglobin	10±12	10±12

Serum ALT was higher in 27 (84.37%) anti-HDV+ve Patients than who were anti HDV-ve Patients 5 (15.63%). While decline in serum Albumin & Hb was almost same in both groups.

Hepatomegaly was present in 62 (30.1%) patients remaining have normal liverspan evidenced by Ultrasound. As shown in Table 2.

DISCUSSION

The Hepatitis D, Co-infection is increasing in Pakistan, being high prevalent country for HBV infection, preventive strategies against HBV infection seem to be insufficient.

The global epidemiology of hepatitis D is changing, on one hand the incidence of hepatitis D virus infection in traditionally prevalent areas of southern Europe e.g italy has declined form 23% to 8.3%. over a period of 10 year form 1987 to 1997[10-12.] .

The results of our study shows the HDV +ve cases serologically 15.1% which is lower as compared to some Pakistani studies [9-13] .

Kirpal Das, Hassan ali et,al , showed the overall sero+ve rate of anti HDV 31.5% in a study conducted at JPMC Hospital Karachi in 2008[4.]

Mumtaz et al reported he prevalence of anti-HDV+ve in Pakistan 16.6%[5.,] some authors stated that a large ratio exists in middle of the county ranging from 20-60-% [13].

Our study showed , the direction relation of HDV infection with markers of chronic HBV infection .

For example in anti-HBe+ve Pt: HDV superiofeation was found in 62%Pt: with low rate of HDV replication (12.1%).

Lee et al reported that HBV, DNA was detected in 62% of their Patients: without HDV superirfection while it was detected in only 10% of Patients with HDV super infection [14].

These results, show that HDV suppresses the replication of HDV genome and HBV-DNA to very low of undeletable levels [15-16] .

Various studies reported that Pt: that chronic HDV show severe chronic Hepatitis1[-15]. In our study we observed significantly high ALT in pt: with HDV super infection (27/32 %).

This is almost same with most of previously studied conducted & deferent places of the Pakistan and the world [14-15-16]

CONCLUSION

Increasing rate of HDV infection is observed in our area, making the HDV related liver diseases more severe.

Our recommendations are, to prevent HBV infection with vaccine & personal hygienic care. Every HBs+ve Patient: should be screened for anti-HDV super infection.

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Original Article

The PMF (Pulmonary massive Fibrosis) and the Exposure period to the Respirable Coal Dust

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ABSTRACT

Objective: To determine the association between pulmonary massive fibrosis and duration of dust exposure in patients with coal worker pneumoconiosis.

Study Design: A cross sectional descriptive study.

Place and Duration of Study: This study was carried out in the Medicine department of Saidu Teaching Hospital Saidu Sharif swat from Jan 2007 to Dec 2011.

Materials and Methods: One hundred and twenty (120) patients suffering from coal worker pneumoconiosis were included**.** They were either already diagnosed patients of coal worker pneumoconiosis or newly diagnosed symptomatic patients.

Results: Forty four(36.6%) had simple coal worker pneumoconiosis, Forty six (38.3%) had complicated coal worker pneumoconiosis and thirty (25%) had PMF, in which twenty patients(66.6%) had exposure of more than twenty years. The results were analysed using the chisquaretest with a p value of 0.00000472.There is clear association between PMF and exposure period to the respirable coal dust.

Conclusion: We conclude that prolonged period of exposure has association with the development of PMF.

Key Words: Coal dust, pneumoconiosis, PMF (pulmonary massive fibrosis).

INTRODUCTION

Coal worker's pneumoconiosis is a progressive parenchymal lung disease [1]. It is caused by the inhalation of respirable coal dust [2]. This dust contains fibrogenic material like Iron and Pyrite [3]which initiates an inflammatory response by the release of different cytokines[4,5]. The fibroblast growth factor and transforming growth factor are considered the main cytokines for causing fibrosis [6]. Based on the radiological features coal worker's pneumoconiosis is divided in threeCategories (I) Simple coal worker pneumoconiosis,(II) complicated coal worker pneumoconiosis(III) Pulmonary massive fibrosis abbreviated as PMF.[7]

In simple coal worker pneumoconiosis pulmonary nodules are less than 1cm in size and dominating the upper lobes.In complicated coal worker pneumoconiosis there are multiple nodules and the size of each nodule is more than 1cm.In PMF the nodules are more than 1cm in size and they fuse together. The period of exposure as well as the concentration of respirablecoal dust is important in the working environment[8] .Lack of preventive measures and prolonged exposure has an impact on the final outcome [9].However all those who are exposed don't develop coal worker pneumoconiosis and PMF, So other factors may be interplaying like smoking, working in small mines (employing less than 50 people),[10, 11] and genetic factors [12, 13].

In developed world the condition is detected earlier through Coal worker X-ray surveillance programme(CWXSP), and every coal worker has to undergo X-Ray examination every five years [14] .PMF is a major health problem in our country because effective legislation and preventive measures are lacking. This study was done to establish the association between PMF and duration of exposure to the respirable coal dust.

MATERIALS AND METHODS

This study was done from Jan 2007 to Dec 2011. A total of 120 patients were included in the study. They were either already diagnosed patients of coal worker pneumoconiosis or newly diagnosed symptomatic patients.The history, age at which exposure started and stopped, duration of exposure, smoking status, the use of face mask during mining, the old x-ray finding, and new x-ray findings were recorded.

At the end of study period X-Ray findings were classified as (I) simple coal worker pneumoconiosis, (II) complicatedcoal worker pneumoconiosis (III) PMF. As the exposure period was variable we operationalized this variable by dividing it in to three groups:

(I)Exposure less than 10years at work place (II) Exposure between 10-20 years at work place

(III)Exposure more than 20 years at work place .The results and association between exposure and PMF were statistically analysed using the chi square test of independence.

RESULTS

All patients (120) were males. The age was ranging from 25 years to 60 years.80% patients belonged to Shangla district while 20% belonged to different parts of malakand division. All patients had active exposure

at work place mainly at underground levels. Minimum age of exposure was 15 years and maximum at which exposure started was 40years.Minimum age at which exposure stopped was 25 years and maximum age at which exposure stopped was 60 years. Minimum period of exposure was 5 years and maximum period of exposure was 25years.

80% patients developed symptoms while still at work while 20% developed symptoms after leaving the work place.85% patients were not using any face mask. Main symptoms were chest tightness and shortness of breath. Forty fourpatients (36.6%) had simple coal workerpneumoconiosis, Forty six patients (38.3%) had complicated coal workerpneumoconiosis and thirtypatients (25%) had PMF (pulmonary massive fibrosis).

When the category of patients with PMF (N=30) was further analysed it was found that 20(66.6%) had exposure of more than 20years, 6(20%) had exposure of 10-20 years and only 4(13.3%) had exposure of less than 10years.

Table 1 shows that prolonging the period of exposure increases the chances of PMF. Although 13.33% patients with PMF had exposure of less than 10 years. When the results were statistically analysed using the chi square test (χ^2=30.77 ,df=4) the observed and expected values are given in the table 2. The p value was calculated to be 0.00000472 suggesting statistically significant association between PMF and exposure period to the respirable coal dust.

The results in the parenthesis are expected values which are close to the observed values.

Table No.1: Categories of coal worker pneumoconiosis and association with the exposure period in years.

Groups	No	Exposure in years	Simple coal worker pneumoconiosis No (%)	Complicated coal worker pneumoconiosis No (%)	PMF No (%)
I	59	<10	29(65.9%)	26(56.52%)	4(13.33%)
II	25	10-20	10(22.72%)	9(19.56%)	6(20%)
III	36	>20	5(11.36%)	11(23.9%)	20(66.66%)
Total	120		44(36.6%)	46(38.3%)	30(25%)

Table No.2: Period of exposure and development of PMF

Groups	No	Exposure in years	Simple CWP	Complicated CWP	PMF
			Observed (Expected)	Observed (Expected)	Observed (expected)
I	59	<10	29(21.6)	26(22.6)	4(14.8)
II	25	10-20	10(9.17)	9(9.58)	6(6.25)
III	36	>20	5(13.2)	11(13.8)	20(9.00)
Total	120		44	46	30

cwp=coal worker pneumoconiosis, PMF= Pulmonary massive fibrosis

DISCUSSION

Coal worker pneumoconiosis and PMF are serious health problems. All our patients were males because females are not involved in mining industry at present. However many other studies have shown that males are dominating this profession[15]. All our patients were symptomatic because they seek medical advice late and we are lacking in enforced X-rays surveillance program .Majority of our patients belonged to Shangla district. The reason is that majority of the labour go to Baluchistan and other parts of the country for coal mining. Majority of these patients were not using any face mask and were working under unprotected conditions which increased the chances of development of PMF [15, 16].In this study 25% had PMF and out of this 66.6% had exposure period of more than 20 years. This percentage is higher than some other studies carried out in USA [15, 16].This may point to the poor working conditions and high concentration of the dust and failure to detect cases earlier[16].Moreover there is lack of education and lack of awareness about the hazards of coal dust.This has also been shown by the study of Sadia Ashraf[17].Awareness on the part of family physicians and GP is also important, as majority of coal worker pneumoconiosis patients may be minimally symptomatic[18].However progression may occur after stopping working at coal mines [19].So regular follow up is necessary.There are limitations to this study. This is not a multicentre study and was carried out in one of the tertiary care hospital of malakand division and not necessarily represents the whole of the country. Moreover it is not possible to directly inspect the working conditions as most of the coal mines are in Baluchistan and tribal areas.

CONCLUSION

We conclude that PMF has close association with the duration of exposure to the coal dust.

Recommendation:

Effective X-Ray surveillance programme to detect the cases earlier, laws to enforce the use of face mask at

work place and to build residential colonies away from the mines.

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Original Article

Protective Role of Magnesium Sulphate in Dexamethasone induced Histopathological Alteration in Spermatogenic Cells of Albino Rats

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ABSTRACT

Objective: This study has been undertaken to assess the spermatoprotective role of magnesium sulphate ($MgSO_4$) on the histology of the seminiferous tubules in dexamethasone induced spermatogenic cells damage in albino rats.
Study Design: Prospective experimental study.
Place and Duration of Study: This study was conducted at the Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi from April 2012 to May 2012.
Materials and Methods: Thirty male albino rats of 90-120 days of age and around 200-250 grams of weight were selected and divided into three groups (A, B&C). Each group comprising of ten rats. Group-A served as control, group-B was given dexamethasone (Dexa) at the dose of 4mg/kg/day intraperitoneally for 20 days. Group-C was administered $MgSO_4$ at the dose of 20mg/kg/day intramuscularly and Dexa at the same dose as given in group- B. The rats were sacrificed at the end of the experimental period and histopathological changes in the germ cells were recorded.
Results: The microscopic examination of group-B rats revealed marked changes in most of the seminiferous tubules such as, vacuolization, detachment of basement membrane, atrophy, sloughing, widening of the interstitial spaces & disorganization of the spermatogenic cells series. Group-C which was protected with magnesium sulphate, showed restoration of basement membrane and spermatogenic cell series.
Conclusion: The present study concluded that magnesium sulphate ($MgSO_4$) administration reduced the damaging effects of dexamethasone in testes.
Key Words: Dexamethasone (Dexa), Magnesium sulphate ($MgSO_4$), Testicular tissue.

INTRODUCTION

Spermatogenesis is a process that involves an array of cellular and biochemical events, collectively culminating in the formation of haploid spermatids from diploid precursor cells known as spermatogonia[1]. This highly regulated and complex process of germ cell proliferation and differentiation leads to the production and release of spermatozoa from the testes, depending upon hormonal stimulation as well as dynamic interaction between the sertoli cells and the germ cells of the seminiferous epithelium[2]. It involves four key cellular events, namely; spermatogoniogenesis, spermatocytes differentiation, spermeiogenesis and spermiation[3].

Normal spermatogenesis represents a precisely regulated balance between continuous cell proliferation and concomitant programmed cell death (PCD), the apoptosis,[4,5] this PCD is required to ensure cellular homeostasis[6]. When the testicular environment cannot support spermatogenesis, specific pathways are accelerated leading to germ cells apoptosis[7]. This abnormal apoptosis of germ cells may lead to an imbalance of cell proliferation and death, resulting in impaired spermatogenesis[8].

Glucocorticoids (GCs) are the major steroid hormones prescribed by the physicians to treat many inflammatory conditions. More than thirty steroids have been isolated from the adrenal cortex in which cortisol is the principal GCs in human and is secreted under the control of hypothalamic-pituitary-adrenal axis[9]. Dexamethasone (Dexa) a synthetic GC which is thirty times more potent than cortisol has made it an especially important drug for stimulating specific glucocorticoid activity[10]. Experimental studies have shown that excess GCs have damaging effects on spermatogenic cells i.e. reducing serum testosterone level[11], impair luteinizing hormone signal transduction and steroidogenesis in Leydig cells of adult rats[12], and also suppress the activity of hypothalamic-pituitary-gonadal (HPG) axis[13].

Minerals play a diverse role in the body. They most commonly function as essential coenzymes and cofactors for metabolic reactions and thus help support basic cellular reactions i.e., glycolysis, the citric acid cycle, lipid and amino acid metabolism, required to maintain energy production and life .They are also important in the regulation of metabolism, gene expression and may influence the development and progression of many chronic diseases[14,15]

Magnesium (Mg) is the second abundant intracellular cation after potassium (K),[16] functioning as a cofactor for more than 300 enzymes. It is essential for all energy-dependent transport system, glycolysis,

oxidative energy metabolism, biosynthetic reactions and cell membrane stabilization[17]. Many enzymes require the presence of magnesium ion for their catalytic action, especially enzymes utilizing ATP or those which use other nucleotides to synthesize DNA & RNA[18].Magnesium sulphate has effectively prevented the histopathological alteration in germ cells caused by alcohol[19], torsion[20]and radiation[21].

This study has been undertaken to evaluate the protective role of magnesium sulphate on dexamethasone induced spermatogenic cells damage in albino rats.

MATERIALS AND METHODS

This study was conducted in the department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Center (JPMC), Karachi. Thirty male albino rats 90-120 days of age, weighing around 200-250 grams, were obtained from the animal house of BMSI and were kept under observation for one week prior to the commencement of the study. They were housed in a temperature and light controlled room and fed with standard laboratory chow and water. The animals were divided into three groups (A, B&C), each comprising of ten rats. Group-A served as control, group-B received dexamethasone[22] at the dose of 4mg/kg/day intraperitonealy for twenty days. Group-C was administered dexamethasone and magnesium sulphate[23], at the dose of 20mg/kg/day intramuscularly for the above mentioned period. At the end of study period, the experimental and corresponding control animals were sacrificed under ether inhalation. Lower midline incision was given and extended up to the skin of the scrotum. The testes were dissected out carefully from each animal without damage to tunica albugina and were fixed in Bouin's fixative for 24 hours. After 24 hours each testis was cut longitudinally into two equal halves and post fixed in fresh Bouin's fluid for next 24 hours. After fixation, they were kept in 70% alcohol overnight. Dehydration was done with ascending strength of alcohol, with changes of one hour each i.e. 80%, 90%, 95%, absolute-I& absolute-II. The tissue was cleared in two changes of xylene for one hour each, and then infiltrated in two changes of paraffin in the laboratory oven at 59 degree centigrade, then paraffin blocks were made & 5micron thick sections were cut with the help of a rotatory microtome. Sections were mounted on labeled glass slides and stained with periodic acid Schiff (PAS) iron hematoxylin[24] for histological study of spermatogenic cells.

RESULTS

Group-A: Testicular sections from control animals revealed that the parenchyma of testes was formed of rounded seminiferous tubules. Most of them attained narrow lumina and lined by stratified germinal epithelium. The epithelium was formed of several types of spermatogenic cells: spermatogonia, primary spermatocytes, spermatids and Sertoli cells. Spermatogonia appeared as small rounded cells, resting on a thin basement membrane and had rounded nuclei. Primary spermatocytes were larger in size than the spermatogonia with large rounded nuclei. Early spermatids appeared as small rounded cells with paler nuclei. Sertoli cells appeared as column cells with euchromatic nuclei and prominent nucleoli in between spermatogonia. The tubules were separated by the interstitial spaces containing groups of interstitial Leydig cells with acidophilic cytoplasm (Fig-1).

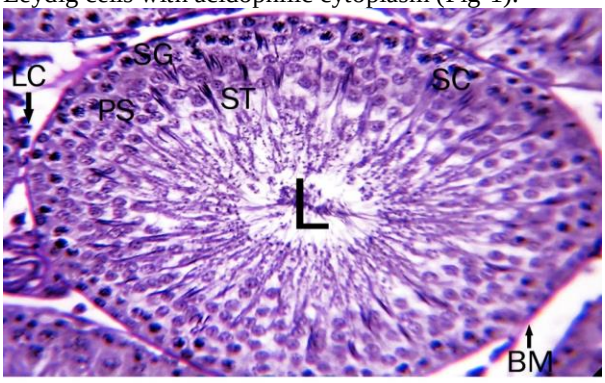

Fig-1
PAS- Iron Haematoxylin stained 5 micron thick section of seminiferous tubule of control group showing intact basement membrane (BM), spermatogonia (SG), primary spermatocytes (PS), spermatids (ST), sertoli cell (SC), lumen (L) contained spermatozoa, and Leydig cells (LC), in the interstitial space. (Photomicrograph X 40)

Group- B: Dexamethasone treated sections revealed that seminiferous tubules attained different shapes and lost the normal arrangement of germ cells. The Lumina of the affected tubules contained sloughed germ cells. The basement membrane showed irregularity or detachment and sloughing to vacuolization of seminiferous tubules, contributing to eventual atrophy. The interstitial tissues exhibited groups of Leydig cells and congested blood capillaries (Fig-2).

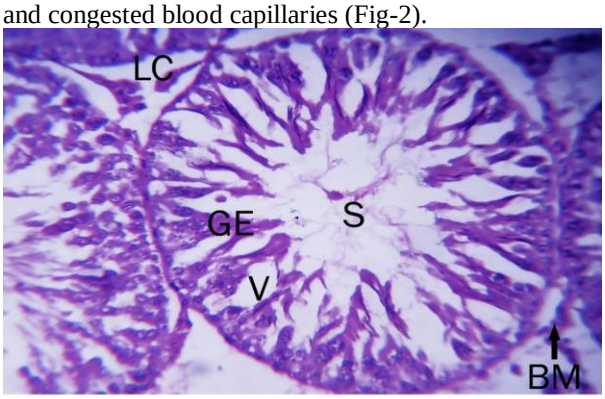

Fig -2
PAS- Iron Haematoxylin stained 5 micron thick section of seminiferous tubule after 20 days dexa treated group , showing disorganized germinal epithelium (GE), vacuolation (V), slough (S) in the lumen and detached basement membrane (BM).(Photomicrograph x40)

Group- C: The morphological examination of testes in group-C revealed seminiferous tubules with slight widening of interstitial spaces but basement membrane was intact. Lumen contained spermatozoa without slough. There was restoration of spermatogenic cell series but some vacuolation was seen (Fig 3).

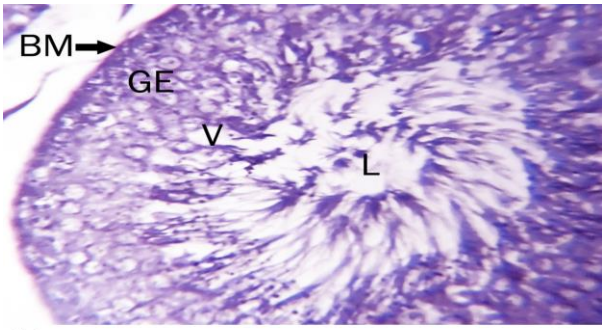

Fig-3
PAS-Iron Haematoxylin stained 5 micron thick section of seminiferous tubule, after 20 days dexa plus magnesium sulphate treated group, showing restoration of germinal epithelium (GE) and basement membrane (BM), lumen (L) contained spermatozoa and some vacuolation (V), Photomicrograph X40.

DISCUSSION

Glucocorticoids are often used therapeutically for their potent anti-inflammatory and immunosuppressive properties in the treatment of allergic, rheumatologic, neurological and autoimmune diseases. [25]

In the present study, examination of the sections of the testes treated by Dexa showed that seminiferous tubules attained different shapes and lost the normal arrangement of germ cell series, along with presence of sloughed germ cells in the lumen. This was due to retraction of the cytoplasmic processes of the sertoli cells, which extend between the different layers of germ cells, so the cells became loosely arranged and easily sloughed out. Nashwa et al (2010)[26] found disorganization of germ cells, vacoulation and sloughing in germ cell of rats, treated with dexamethasone. Orazizadeh et al (2010)[27] also demonstrated Dexamethasone induced histopathological alterations such as epithelial vacuolization, atrophy of the seminiferous tubules and reduction in spermatozoa and apoptosis of germ cells was also significantly increased. Martinez et al (2000)[28] found that intake of alcohol has been associated with marked degenerative changes in germ cells of albino rats, due to its apoptogenic effect mainly by DNA damage, oxidative stress and androgen suppression. The group-B also showed decline in the number of Leydig cells, which might be due to glucocorticoid suppression of luteinizing hormone (LH) signal transduction and steroidogenic enzyme activities. Our findings are in agreement with Sapolsky et al (2000)[11] and Hardy et al (2005)[7], who observed that elevation of glucocorticoid concentration inversely affects testosterone production by reducing the number of Leydig cells through the induction of germ cell apoptosis. The results of Yazawa (2001)[29] is in disagreement of our study who revealed that dexamethasone decreased testicular germ cells apoptosis in ischemic testes, by suppressing oxygen-derived free radicals and its anti-inflammatory effects.

In present study the simultaneous administration of magnesium sulphate with dexamethasone in group-C animals showed restorative effects on germ cells histoarchitecture. This was due to the diverse role of magnesium in metabolic reactions as a co-enzyme and regulator of hypothalamic-pituitary-adrenal axis (HPA-axis), thus it helps to support basic cellular reactions. Adivarekar et al (2005)[20] showed that treatment of torsion by detorsion alone does not prevent testicular damage however administration of $MgSO_4$ prior to detorsion, resulted improvement in semen quality, fertility and reduction in long term morbidity. Chandra et al (2012)[30] demonstrated significant increase in testosterone level along with progressive improvement in the histoarchitecture of genital organs after administration of magnesium sulphate for one and two consecutive spermatogenic cycles in albino rats.. Cinar et al (2011)[31] concluded in his study that supplementation of $MgSO_4$ increases free and total testosterone.

CONCLUSION

The present study shows cytotoxic and apoptotic effects of dexamethasone on the testes of albino rats. The study further emphasizes a definite protective role of simultaneous administration of magnesium sulphate in spermatogenic cells of albino rats.

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Original Article

Comparison of Liver Enzymes and Cardiovascular Risk Factors in Hypertensive and Normal Subjects

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ABSTRACT

Objective: To compare the liver enzymes between hypertensive and normal subjects.
Study Design: Cross-sectional, descriptive study.
Place and Duration of Study: Basic Medical Sciences Institute, J.P.M.C, Nehal Hospital and Shamsi Hospital Karachi, from December 2006 to March 2011.
Materials and Methods: The study has compared the liver enzymes and associated cardiovascular risk factors like blood pressure, BMI, waist hip ratio, blood sugar, lipid profile between 100 normal and 100 hypertensive subjects. The assessment was done by applying independent t test and Pearson correlation using statistical package for social sciences 15.
Results: The normal and hypertensive subjects were compared with liver enzymes, systolic and diastolic blood pressure, lipid profile, BMI and waist/hip ratio. All values showed significant correlation ($P < 0.001$) using independent t test. In the hypertensive subjects all the liver enzymes were found to be raised in comparison with hypertensive but were within their normal ranges. The levels of GGT (Gamma glutamyl transferase) was found to be raised beyond its normal range and was compared according to type I and Type II stage of hypertension and was found to be raised significantly.
Conclusion: Among all the liver enzymes compared with uncontrolled hypertensive GGT was found to be most significantly correlated with all the factors increasing cardiovascular risk, and needs to be measured in every hypertensive individual.
Key Words: Blood pressure. Gamma Glutamyl transferase. Cardiovascular risk factors.

INTRODUCTION

The prevalence of cardiovascular disease and its associated risk factors are increasing worldwide. The recent data collected showed that about one quarter of the worlds population is hypertensive and around 1.15 billion hypertensive patients will be in developing world by 2025 [1].In south Asia the prevalence of cardiovascular disease and its adverse health effects are increasing far more rapidly than in young age group in any other region of the world [2, 3].The main associated risk factors which are linked to this high prevalence are hypertension, diabetes mellitus and obesity.[4]
Gamma- glutamyltransferase (GGT) has always been used as a marker to assess the excessive alcohol intake,[5] It has been recently linked with cardiovascular disease and all cause mortality, suggesting its role as predictor of cardiovascular disease [6]. The role of GGT in cardiovascular risk factor such as dyslipidaemia,[7] hypertension,[8] diabetes mellitus and metabolic syndrome[9] irrespective of alcohol consumption. However the exact mechanism linking GGT with cardiovascular disease is still lacking. Although lot of data on various aspects of hypertension and liver enzymes has been published in western world, very few if any such study has taken place in this part of the world. In this study we aim to evaluate the levels of liver enzymes in general and GGT in particular with hypertension and its associated risk factors. The studies also compare liver enzymes in normal subjects.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology, B.M.S.I., J.P.M.C, Karachi and secondary care hospitals of Karachi Nehal General Hospital Malir Kala Board Karachi and Shamsi General Hospital Shamsi society near wireless gate Karachi. The study was done initially from December 2006 to 2008 and was then further extended to March 2011.
The present study was cross-sectional study, 100 normal subjects and 100 hypertensive subjects were selected. The inclusion criteria was adult with either gender above 18 years of age. The hypertensive subjects were included by measuring blood pressure or if they were on anti-hypertensive therapy. Subjects with acute or chronic liver, kidney and heart disease, history of alcohol addiction, patients taking drugs affecting liver enzymes, patients suffering from cancer, and pregnant women. Subjects with hepatitis C virus antibody and hepatitis B virus surface antigen and patients with aspartate amino transferase (SGOT) and alanine amino transferase (SGPT) and Gamma Glutamyltransferase (GGT) levels more than three times normal and subject with total leukocyte count more than 10,000/µl were excluded. Hypertension was

defined according to the criteria set by JNC VII classification of hypertension.[8]

A verbal consent of the patients were taken at JPMC and written informed consent of the patients were taken at Nehal and Shamsi hospital. The protocols of the procedure were explained before taking the sample. All participants were asked to fast at least 12 hours and take their medications with their evening meal. They are also instructed to avoid heavy physical activity for at least 2 hours before examination. Height and weight was measured with the help of height and weight scale ZT-120. Weight was measured in standing position without shoes while the shoulder was in normal position. BMI was calculated as weight in kilograms divided by height in meters square. Among the measurements of abdominal obesity, high waist circumference was defined > 90 cm in males and > 80 cm in females. After a 5 minute rest blood pressure was measured in sitting position. History of daily physical activity, addiction, previous illnesses and types of medication use was also noted. Reference range of values, in our laboratory, are 0–40 IU/l for ALT, 0–37 IU/l for AST, 0–50 IU/l for GGT. High cholesterol (TC), high triglyceride (TG), high low density lipoprotein cholesterol (LDL), and low high density lipoprotein cholesterol (HDL) were defined as TC ≥ 200 mg/dl,TG ≥150 mg/dl, LDL-C ≥ 130mg/dl, and HDL-C ≤ 40 mg/dl according to ATP III.[9]Eight milliliter of venous blood was drawn with a disposable syringe. Two milliliter was transferred to EDTA containing tube for CBC and remaining blood was stored for collection of serum. Complete Blood Count was done by Automated cell counter SYSMEX KX 21. Blood sugar was done by GOD-PAP Enzymatic Colorimetric Method. Tests for the detection of liver enzymes were performed on Microlab 300 Merck by enzyme kinetic method, the kit by Bioscience (Spain) were used. Hepatitis C virus antibodies are detected by chromatographic immunoassay (LG Quick card). Hepatitis B surface antigen is detected by qualitative immunoassay (Abbot Laboratory).

Statistical Analysis: Data analysis was done on Statistical Package for Social Sciences (SPSS) version 15. The statistical significance of difference between the mean values of two groups was evaluated by the students't' test. The difference in the mean values of the two groups was regarded as statistical significant if the P value was less than 0.05 and it was taken as highly significant if P value was less then 0.001. Correlation Coefficient was detected using Pearson coefficient of correlation SPSS-15. Figure was computed on Microsoft excel 2007.

RESULTS

The study included 100 uncontrolled hypertensive and 100 normal subjects consisting of 93 female and 107 male. Table I is shows the comparison of physical parameters between normal and hypertensive groups. The table has shown that patients who were hypertensive have increased levels of GGT with increased waist hip ratio and BMI.

Table No.1: Comparison of Physical Parameters in Normal and Hypertensive

Category	Group	Mean ± Std Deviation	P value
BMI kg/m^2	Control	21.21±1.49	0.000**
	Hypertensive	25.66±1.92	
w/h ratio	Control	0.92±0.27	0.000**
	Hypertensive	0.98±0.58	
Systolic Blood pressure mm of Hg	Control	121.46±10.66	0.000 **
	Hypertensive	163.37±9.81	
Diastolic Blood Pressure mm of Hg	Control	77.91±7.21	0.000 **

n = 100 control subjects and 100 hypertensive subjects (** P = < 0.001, * = < 0.05)

Table No.2: Comparison of Biochemical Parameters in Normal and Hypertensive

Category	Group	Mean ± Std Deviation	P value
FBS mg/dl	Control	88.92±12.29	0.04 *
	Hypertensive	94.24±13.69	
RBS mg/dl	Control	121.46±14.6	0.000 **
Total lipid mg/dl	Control	681.04±54.76	
	Hypertensive	945.10±188.15	
Cholesterol mg/dl	Control	179.46±16.43	0.000 **
	Hypertensive	256.39±62.17	
Triglycerides mg/dl	Control	160.76±12.46	0.000 **
	Hypertensive	216.16±53.89	
HDL mg/dl	Control	42.67±3.67	0.000 **
	Hypertensive	33.63±2.99	
LDL mg/dl	Control	113.44±11.94	0.000 **
	Hypertensive	207.32±47.55	
Creatinine mg/dl	Control	0.87±0.080	0.000 **
	Hypertensive	1.15±0.100	
SGPT IU/L	Control	8.53±1.77	0.000**
	Hypertensive	20.81±12.72	
SGOT IU/L	Control	7.78±1.36	0.000 **
	Hypertensive	10.55±1.56	
GGT IU/L	Control	17.58±6.02	0.000 **
	Hypertensive	55.91±8.27	
ALK Phos-phatase IU/L	Control	125.80±10.33	0.070

n = 100 control subjects and 100 hypertensive subjects (** P = < 0.001, * = < 0.05)

Table 2 is shows the biochemical parameters of lipid profile and serum creatinine and liver enzymes which were found to be raised in hypertensive group when

compared with normal subjects. All the hypertensives have shown rise in lipid profile impaired or rise in blood sugar levels and increases in liver enzymes in comparison with normal subjects.The hypertensives were divided into two groups according to severity of hypertension into type I stage and Type II stage of hypertension JNC VII Fig I and II. Type I group is considered as moderate hypertensive consists of systolic > 140 to 159 mm Hg and diastolic >90 to 99 mmHg. The Type II group is considered as severe hypertensive with systolic >160 and diastolic > 100 mm Hg. The figure I and II were showing the levels of GGT in with respect to rise in blood pressure in stage I and stage II of hypertension. The mean values were compared with systolic and diastolic blood pressure respectively which showed the raised levels of GGT as the blood pressure rises.

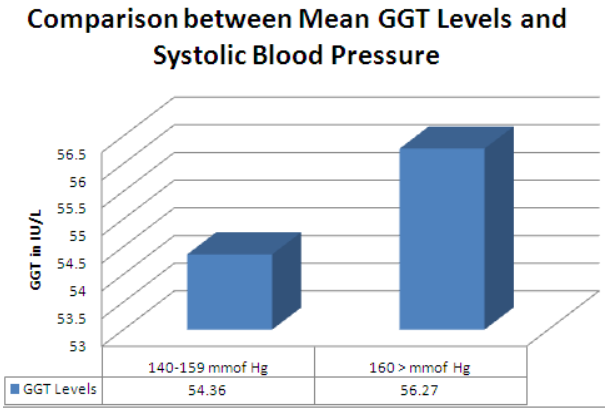

Figure No.I. Comparison of stage I and Stage II systolic blood pressure with GGT levels.

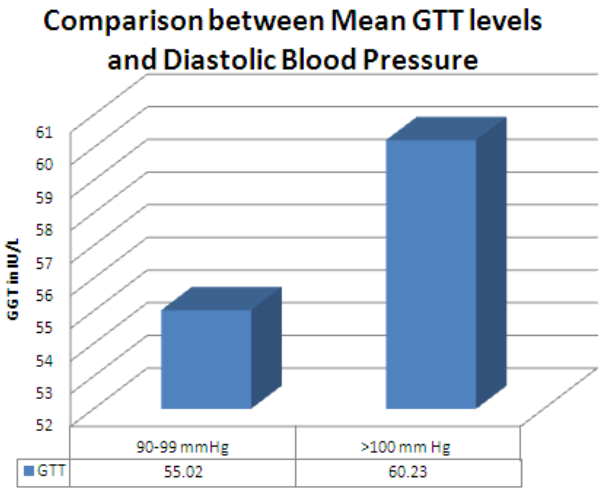

Figure No.2. Comparison of stage I and stage II Diastolic blood pressure with GGT levels.

DISCUSSION

In this study the relationship of liver enzymes with hypertension was evaluated in life time non-alcoholics in both genders. The level of liver enzymes was found to be raised when compared between normal and hypertensive subjects, but all were found to be within their normal range except GGT table I. The results of this study clearly indicate that in hypertensives have raised levels of BMI and waist hip ratio which could be one of the factors of raised levels of GGT in these patients. Similar findings were also founded by studies done elsewhere which are done on nonalcoholics.[10,11]

In this study the levels of GGT were found to be raised in hypertensives with factors favoring obesity (BMI, waist hip ratio), and cardiovascular risk factors (blood sugar, total lipid, cholesterol,triglycerides,LDL and low HDL), conforming with previous studies mainly conducted in European population or among alcoholics [12,13]

The raised levels of GGT was among overweight or individuals with increased waist hip ratio, supports the finding of previous studies [14,15] which have correlate central adiposity as a stronger predictor of elevated liver enzymes especially GGT, as our findings further support the hypothesis that NAFL may represent an important underlying mechanism for the observed associations between GGT and Hypertension. In this study the relationship between raised GGT and hypertension was further evaluated by dividing the hypertensive subjects into two groups of Type I stage and Type II stage of Hypertension[8]. Among the group with raised diastolic blood pressure the GGT was found to be significantly raised in comparison with raised sytolicblood pressure.

Arterial stiffness, which is due to change in structural and function characteristics of the vessel wall, has been related as independent predictor of cardiovascular events and mortality [16]

It is persumed that the levels of GGT in the serum may occurs in those individuals with low but persistent increase in oxidative and other cellular stresses. Many experimental studies have indicated the GGT levels are directly involved in the generation of reactive oxygen species in the presence of iron or other transition metals[17,18]. The levels of GGT activity are directly related to oxidative stress which play a leading role in the development of atheromatous plaques and produce oxidation of LDL in the presence of iron ions [19].Gamma-glutamyltransferase activity has been identified in human atheromatous plaques [20].Previous studies have also compared the levels of GGT are with some atherosclerotic risk factors and used GGT levels as a predictors of future heart disease, hypertension,and stroke [21,22.]

Although the exact mechanism responsible for this association is unknown, several possible mechanisms have been proposed for the role of serum GGT in increasing cardiovascular risk. The most widely accepted mechanism is oxidative stress, followed by hepatic insulin resistance and subclinical inflammation. Another reason of elevated serum GGT in patients with hypertension could be due to inflammation due to

atherosclerotic cardiovascular disease [23]. The oxidative processes which presumably can lead to generation of free radicals in the presence of Fe ++ and Cu++ and induce oxidative stress [24].

CONCLUSION

Our findings indicate that the association between GGT and hypertension are not related solely by alcohol consumption. Increase in levels BMI, waist hip ratio, high Cholesterol, triglycerides, LDL and low HDL (as cardiovascular risk factors) can lead to increase in GGT.

However the exact mechanism by which the levels of GGT were found to be raised in hypertension and how it increases the risk factors of cardiovascular diseases are yet to be analyzed and need further studies.

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Original Article

Outcome of Neonatal Tetanus in Hospitalized Patients

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ABSTRACT

Objective: To determine the outcome of neonatal tetanus in hospitalized patients.

Study Design: A hospital based cross sectional study.

Place and Duration of Study: This study was conducted in Children Hospital Quetta from April 2011 to March 2012.

Materials and Methods: A hospital based cross sectional study was conducted to determine the outcome of neonatal tetanus. 60 full term neonates from 0 to 28 days of age were included in the study after fulfilling the criteria of tetanus. Diagnosis was established exclusively on clinical grounds.

Results: Mean age of presentation was 7.5 days, male female ratio was 3:1. Most common presentation was generalized seizure in 51. 5 % cases, 30.1 % presented with lock jaw, 15.1% presented with opisthotonos and only 03. 3% presented with poor sucking. 92 % mothers were illiterate, 85% belong to the low socio economic status, 78% were from rural area, 75% delivered at home, immune status was low in 70% mothers, cord was cut by non sterilized equipments in 65%, cord was tied with unclean thread in 60%, unhygienic material was applied to the cord in 54%, and 25% developed tetanus after circumcision done by non sterilized instruments at home. 25 out of 60 neonates died and the overall mortality rate was 40.1% out of 60 cases, 24 were put on ventilator and 9 of them (37.5%) died, while out of 36 unventilated cases 16 (44.4%) died.

Conclusion: The findings of the study demonstrate that the high mortality rate of neonatal tetanus is due to lack of knowledge of risk factors. Lack of maternal education, low immune status of mothers against tetanus along with unsafe and unhygienic delivery practices are major risk factors responsible for the development of neonatal tetanus.

Key Words: Neonates, Tetanus, Umbilical cord, Outcome.

INTRODUCTION

Tetanus is derived from Greek word Tetanos "taut", and Teinein "to stretch"[1]. It is a medical condition characterized by a prolonged contraction of skeletal muscle fibers caused by a neurotoxin produced by Gram Positive, anaerobic bacterium Clostridium tetani. Tetanus account for approximately 36 % 0f neonatal mortality worldwide[2]. Neonatal tetanus is the disease of developing countries and 0.5% of total neonates die of this disease every year[3]. Neonatal tetanus is a major health problem in Pakistan too, being one of the common causes of deaths especially in rural settings[4]. Neonatal tetanus usually occurs through infection of umbilical stump, particularly when the stump is cut with a non-sterile instrument. Incubation period of neonatal tetanus is 4 to 14 days after birth averaging 7 days. The shorter the incubation period, the more severe the signs[5]. Tetanus often begins with mild spasm in the jaw muscles (lock jaw). The spasm can also affect the chest, neck, back and abdominal muscles. Back muscles spasm often cause arching, called opisthotonus. Poor sucking, irritability, spasticity and opisthotonos are the most common signs and symptoms[6]. Diagnosis of neonatal tetanus is exclusively on clinical grounds with the high index of suspicion. Laboratory tests are useful only to exclude other diseases like sepsis, meningitis and metabolic fits[7]. Mortality tends to be very high, in absence of medical treatment case fatality approaches 100%, with hospital care 10 -60% of cases die, depending upon the availability of intensive care facilities[8]. In developing countries, little is known about risk factors of neonatal tetanus. Maternal immunization status is very important in protection of neonatal tetanus. Tetanus toxoid is actively transported by the placenta from an immunized mother to her fetus providing passive protection against tetanus during the neonatal period and the following month or two of life[9]. Immunization of pregnant women or women of child bearing age with at least two doses of tetanus toxoid is estimated to reduce the mortality from neonatal tetanus 94%[10]. Even before tetanus vaccine available, neonatal tetanus became increasingly rare in most of Europe and North America through hygienic childbirth practices and cord care[11]. This means the factors other than maternal immune status are also play an important role in development of neonatal tetanus. These factors include type of delivery surface[12]; cord care[13], infants bathing practices, attendant's hand washing practices, skin to skin contact between mother and newborn. Some other factors such as maternal literacy level, socioeconomic status and ethnicity are also important. Tropical use of antiseptic (chlorhexidine) to the cord found to be effective in lowering the incidence of neonatal tetanus[14].

MATERIAL AND METHODS

A hospital based cross sectional study was conducted during April 2011 till March 2012. It is conducted to in the Neonatal Intensive Care Unit (NICU) of Children Hospital Quetta after due permission of chief executive of CHQ as it is the NICU of tertiary care unit with best nursing care and instrumental facilities including mechanical ventilation. Total 60 neonates who fulfilled the inclusion criteria were included in the study. Inclusion criteria were the, full term neonates from 0-28 days of age presented with generalized seizures, lock jaw, poor sucking and opisthotonos. All these neonates were admitted in NICU. Neonates with hypoxic ischemic encephalopathy, meningitis, sepsis and metabolic disorder were excluded from the study. These cases may act as effect modifiers and if included in the study sample, would have introduced bias in the study results.

Diagnosis of neonatal tetanus based exclusively on clinical grounds. Investigations like serum electrolytes, liver function tests, renal function tests, csf examination, x ray chest and arterial blood gasses were performed during the course of illness when needed. The risk factors, clinical presentation, complications and outcome of these neonates were recorded in predesigned proforma. Data was analyzed on SPSS version 12.

RESULTS

Total 60 neonates included in the study after fulfilling the criteria of tetanus. 48 out of 60 presented within 7 days of life. The mean age of presentation was 7.5 days. Male female ratio was 3:1. Majority (78%) of the neonates came from rural areas. Most common risk factor was maternal illiteracy (92%). A mother was considered illiterate when she has no formal schooling ever, otherwise she was labeled as literate irrespective of their level of education.

Table No.1: Risk Factors

Risk Factors	% age
Maternal illiteracy	92
Low socio economic status	85
Rural areas (lack of medical facility)	78
Home deliveries conducted by dais	75
Low immune status of mothers	70
Umbilical cord cut by knife or unclean blade	65
Umbilical cord tie with unclean thread	60
Application of unhygienic material to cord	54
Circumcision done by unsterilized instrument	25

Low socio economic status (monthly income of family < 10,000 rupees) was also significant in 85 %; parents were unable to bear the expenses of smallest clinic run by the lady health visitors even. Home deliveries (75%) conducted by dais or untrained persons, low immune status (less than 2 doses of tetanus vaccine during pregnancy) of mother was 70%, umbilical cord tie with unclean thread (65%), cord cut by unsterilized equipment as knife siccessor and unclean blade (60%), application of unhygienic material to the cord like ash, mud, surma and mustard oil (54%) also contributing factors. Only 5% neonates developed tetanus through septic wound after circumcision by unsterilized equipments at home. Most of the neonates had more than one risk factors, such as a neonate of illiterate mother came from rural area, belongs to low socio economic status, delivered at home and applied unhygienic material to the cord at the same time. General seizures was the most common clinical manifestation in 31 cases (51.2%), 18 cases (30.1%) presented with lock jaw, 9 cases (15%) presented with opisthotonus and only 2 (3.3%) came with the compliant of poor sucking.

Table No.2: Clinical Manifestations

Clinical	Cases	% age
Generalized seizures	31	51.5
Locked jaw	18	30.1
Opisthotonus	09	15.1
Poor sucking	02	03.3

Table No.3: Complications

Complications	Cases	% age
Aspiration pneumonia	21	35.2
Renal failure	17	28.3
Intractable seizures	13	21.6
Nosocomial infection	05	08.3
Pneumothorax	04	06.6

Table No.4: Outcome Total: 60

Total	Mechanical ventilated cases		Unventilated cases	
60	24		36	
Expired	Expired	Percent	Expired	Percent
25 (40.1%)	09	37.5	16	44.4

Regarding the outcome, 25 out of 60 neonates were died with overall mortality rate 40.1%. Out of 60 neonates 24 were put on mechanical ventilation after due consent from their parents, 09 were expired and the mortality rate of ventilated neonates was 37.5%, while 16 out of 36 unventilated neonates were expired and the mortality rate of unventilated neonates was 44.4%. Mechanical ventilation did not make any significant difference in outcome of ventilated and unventilated neonates. Most common complication was the aspiration pneumonea in 21 (35.2%) cases, 17(28.3%) developed renal failure, 13(21.6) had intractable seizures, nosocmial infection developed in 5(8.3%) cases. Only 4 (6.6%) had pneumothrox, basically pneumothorax was the complication of mechanical

ventilation as all of them who developed pneumothorax were on mechanical ventilation.

DISCUSSION

Mortality of neonatal tetanus remains as important, yet preventable cause of neonatal mortality. The overall mortality in this study is 40.1% , which is consistent to other studies of Pakistan 44% in Lahore[15], 30.1% in Dadu[16], 43.7% in Bahawalpur[17], 32per 1000 live birth in Loralai (Balochistan)[18]. In the study of Nigeria and Kenya mortality was 20.6[19]and 21per 1000 live births[20]. Although neonatal tetanus accounted for half of all neonatal deaths and one fourth of all infant mortality in some countries during 1980s[21], the situation has not changed much in Pakistan, as was responsible for 38% of neonatal and 18% of all infant mortality. Mortality rate of ventilated neonate in this study was 37.5% and unventilated 44.4%; means mechanical ventilation did not make any significant difference in outcome of neonatal tetanus. Cause of high mortality of neonatal tetanus in Pakistan is because of lack of knowledge of risk factors. Maternal illiteracy (92%) and low socio economic status (85%) were found to be more common risk factors in the study. Due to maternal illiteracy mothers are unaware of the complication of home deliveries by untrained dais under unhygienic condition found in 75%. Because of low socio economic status parents could not approach to even the cheapest private clinics in rural areas where the free medical facilities are not available at Government level. Other important risk factors are cord cut by unsterilized instrument such as knife, scissor and unclean blade in 65%, cord tie with unclean thread in 60%, unhygienic material (ash, mud mustard oil) applied to the cord in 54%. Only 25% developed tetanus after circumcision done by unsterilized instruments. These risk factors are consistent to the study conducted by quddus ref[18]. Aspiration pneumonia, renal failure and intractable seizures were the common complications found in 35.2 %, 28.3% and 21.6% respectively. 8.3% developed nosocomial infections and 4% had pneumothorax after mechanical ventilation. The results of this study revealed that neonatal tetanus is more common in deliveries conducted by untrained persons under unhygienic conditions in rural areas where the immunization status of mothers are also not up to the mark. Neonatal tetanus can be prevented by educating the general public about the risk factors and preventive measures of this fatal disease. Health personal should create awareness at community level and counseling of pregnant women at individual level to encourage safe delivery practices. Free health facilities should provide to the poor communities of rural areas for safe deliveries by trained persons under hygienic condition and better status of immunization of pregnant women against tetanus.

CONCLUSION

The findings of the study demonstrate that the high mortality rate of neonatal tetanus is due to lack of knowledge of risk factors. Lack of maternal education, low immune status of mothers against tetanus along with unsafe and unhygienic delivery practices are major risk factors responsible for the development of neonatal tetanus.

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Original Article

Relationship of Child-Pugh Classification with Liver Function Tests and its Clinical Implication in Patients of Chronic Liver Disease

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ABSTRACT

Background: Child-Pugh classification currently remains the most important parameter to determine liver function in patients of chronic liver disease (CLD). This study was carried out to find a relationship between abnormal Liver Function Tests (LFTs) and extent of liver damage in patients of CLD grouped as Child class A and B.

Aims and objectives: To find a relationship between LFTs and severity of liver disease assessed by Child-Pugh scoring.

Study Design: Retrospective study.

Place and Duration of Study: This study was conducted at the Medical Words of Services Hospital, Lahore from February 2009 to June 2009.

Materials and Methods: It was a retrospective analysis of 40 patients aged 17-74 with CLD. Patients were selected from medical wards of Services Hospital Lahore. Patients were classified as Child class A and B on the basis of severity of liver function. Liver function tests including prothrombin time(PT), serum bilirubin, enzymes like Alkaline Phosphatase (ALP), Aspartate Transaminase (AST), Alanine Transaminase (ALT), serum Proteins and Albumin concentrations were performed by standard laboratory methods.

Results: It was observed that serum level of ALP, ALT, AST and the AST/ ALT ratio as well as prothrombin time were significantly increased in patients as compared to their controls. On the other hand level of total proteins and albumin were significantly decreased in patients as compared to their controls whereas the level of bilirubin remains insignificant.

In Child class B patients the levels of serum bilirubin, ALP, ALT, AST and ratio AST/ALT were increased as compared to these parameters in Child class A patients. It was observed that level of serum ALP and ALT were non significantly and level of serum bilirubin, AST and AST/ALT ratio were significantly increased in Child class B patients as compared to the patients of Child class A. On the other hand level of serum total proteins and albumin were significantly decreased in Child class B patients as compared to patients of Child class A. Prothromin time is significantly increased in Child class B patients as compared to the patients of Child class A.

Conclusion: Further deterioration in LFTs may warn a clinician about progress of disease in a patient of CLD and to further investigate about the liver function at that stage.

Key Words: Liver function test, Child Pugh classification, chronic liver disease (CLD).

INTRODUCTION

Interpreting abnormal liver function tests (LFTs) and trying to diagnose any underlying liver disease is a common scenario in Primary Care. These tests can also be used to distinguish among different types of liver disorders, guage the extent of known liver damage, and follow the response to treatment[1].

Most common liver function tests like serm bilirubim, albumin, and prothrombin time can indicate liver damage. Prothrombin time may help to measure the liver's ability to synthesize platelets. Prothrombin ime may be elevated in hepatitis and cirrhosis[2]. Elevated aspartate aminotransferase and alanine aminotransferase level associated with hype bilirubinemia in cirrhosis are observed[3]. Ratio of AST/ALT is biomarkers of liver injury in a patient with some degree of intact liver function[4]. The AST/ALT ratio is a dependable marker of stage of fibrosis and cirrhosis[5]. In chronic liver disease AST>ALT once cirrhosis established. The extremes of AST/ALT ratio are also helpful; ratio more than 2 suggests alcoholic liver disease, and a ratio of <1 suggests nonalcoholic disease[6'7].

Srum bilirubin convertration was independently correlated with bleeding time, suggesting that liver function has an important role in determining primary haemostasis in patients with cirrhosis[8].Serum bilirubin, albumin, and prothrombim time are altered only in patients with advanced liver disease[9]. Albumin concentration is diminished in patients with liver failure and this may be due in part to its detoxifying capabilities[10].

Among the evaluation approaches of liver function, including aminotransferases, bilirubin, albumin, prothrombin time, currently Child-Pugh classification remains the most important method to determine the prognosis of liver function, especially in patients of

chronic liver disease. However, all these approaches have their limitations[11].

MATERIALS AND METHODS

Statistical analysis: Data was analyzed by using SPSS-18.0. Quantitative variables like prothrombin time, serum bilirubin, enzymes like alkaline phsophatase, aspartate transaminase, alanine transaminase, serum protein and albumin were reported as mean ± S.D. Variables were calculated compared with controls using student 't' test. P values of < 0.05 was considered statistically significant.

RESULTS

Levels of serum bilirubin, ALP, ALT, AST and their ratio were increased in patients as compared to these of controls. It was observed that level of serum bilirubin was not significantly increased. On the other hand level of ALP, ALT, AST and their AST/ALT ratio were significantly (P<0.001) increased as compared to their controls. Level of total protein and albumin were significantly decreased (P<P0.001) in patients as compared to controls. Prothromin time is increased non significantly in patients as compared to that of controls (Table 1). Levels of serum bilirubin, ALP, AST and AST/ALT ratio were increased in patients of Child class B patients as compared to these parameters of Child class A patients. It was observed that level of serum ALP and ALT were non significantly affected. On the other hand level of serum bilirubin, AST and AST/ALT were significantly (P<0.001) increased in Child class B patients a compared to the patients of Child class A. Level of serum total protein and albumin were significantly decreased (P<0.001) in Child class B patients as compared to patients belong to Child class A. Prothromin time is significantly increased (P<0.001) in Child class B patients as compared to the patients of child class A (Table 2).

Table No.1: liver function test in Child class A and class B groups

Lever Function test	Total Cases	Controls(20)
Serum Bilirubin (mg/dl)	2.13±1.76**	0.46±0.29
ALP (U/L)	266.8±96.46**	95.5±20.93
AST (U/L)	59.4±23.92**	25.3±3.08
ALT (U/L)	43.0±12.95**	27.0±8.24
AST/ALT ratio	1.40±0.47**	0.97±0.15
Total Protein (gm/dl)	6.30±0.55*	7.4±0.43
Albumin (gm/dl)	3.3±0.56**	4.2±0.26
PT (seconds)	14.0±2.34	13.1±4.01

**P^0.001= Highly significant difference.

Table No.2: Liver function test in Child Class A and Class B Groups

Liver Function test	Child Class A (13/32.5%)	Child Class B (27.67.5%)	Controls (20)
Serum bilirubin (mg/dl)	0.92±0.34	2.7±1.9**	0.46±0.29
ALP(U/L)	232.2±94.26	283.4±94.72	95.5±20.39
AST(U/L)	43.2±9.15	67.2±24.98**	25.3±3.08
ALT U/L)	38.8±8.2	45.0±14.4	27.0±8.24
AST/ALT Ratio	1.15±0.32	1.52±0.49**	0.97±0.15
Total Protein (gm/dl)	6.6±0.27	6.1±0.58**	7.4±0.43
Albumin (gm/dl)	3.6±0.36	3.2±0.60**	4.2±0.26
PT(seconds)	12.2±0.44	14.82±2.42**	13.1±4.01

**P<0.001= Highly significant difference.

DISCUSSION

Long standing liver diseases like hepatitis, continued toxic insults of liver like alcohol or chronic drug use, damage from free radicals etc. result in formation of scar tissue or cirrhosis. This results in compromised liver function[12].

Levels of serum bilirubin and ALP were increased in patients as compared to controls in our study . This was in contrast with a study who found that marked elevation of Alkaline Phosphatase is observed only in biliary cirrhosis[13]. Other study found that increased level of serum bilirubin and Alkaline Phosphatase indicate some type of liver dysfunction resulting in liver tissue damage. However level of serum bilirubin and ALP are predictors of poor prognosis[14]. Another study found that severity of liver disease is assessed by bilirubin concentration[15].

Present study is in accord with a study who observed an elevated level of AST, ALT and their ratio in patients of CLD. Study reported that ALT and AST both use pyridoxine as a coenzyme, but the synthesis of ALT is more strongly inhibited by pyridoxine deficiency than is the synthesis of AST[16]. Present study observed that the level of AST>ALT. a group of workers reported that although ratio of AST:ALT> or = 1 is highly specific but not diagnostic for the presence of cirrhosis[17,18]. The ratio reflects the grade of fibrosis in these patients. Our results are in contrast to the study who observed that once cirrhosis is established, ALT>AST.

Present study observed significant increased ratio AST/ALT i.e. 1.25 in patients with cirrhosis as compared to their controls. It is reported that a ratio of AST/ALT>1 suggested cirrhosis. This ratio is used to distinguish cirrhotic patients with chronic HCV infection from noncirrhotic patients and also used to

correlate the ratio with the grade and stage of hepatitis and other biochemical indices[18,19].

Level of total protein and albumin were significantly decreased (P>0.001) in patients as compared to their controls. A study suggested marked dysfunction of albumin function in advanced cirrhosis[20]. Our study observed a non significant increased level of Prothromin time in patients as compared to their controls. Longer prothrombin time was also observed in a study which may indicate some type of liver dysfunction resulting in liver tissue damage[15].

In the present study 32.5% patients fell into the Child class A, 67.5% in class B. A study reported that once patients with any type of liver disease fall into the Child-Pugh class B or class C category, survival is significantly reduced and transplantation should be considered[21].

It was observed that level of serum ALP and ALT were non significantly increased in child class B patients as compared to Child class A patients. On the other hand, level of AST and AST/ALT were significantly (P<0.001) inreased in child class B patients as compared to patients of child class A. A study reported that the markers of hepatocyte injury and inflammation are AST and ALT[22]. However a study reported that markers of hepatocellular injury, AST and ALT lack some specificity because they are found in skeletal muscles too[23]. Another study stated that the ratio of AST/ALT provides prognostic information independent of Child-Pugh class in cirrhosis[24].

Level of serum bilirubin, serum total protein and albumin were significantly decreased (P<0.001) in Child class B Patietns as compared to patients of Child class A. It is reported that hepatic function can be assessed by applying the values for albumin, bilirubin and prothrombin time in the modified Child-Pugh grading system. Serum albumin level can serve as an index of liver synthetic capacity. Low albumin is most often caused by acute or chronic liver disease[25]. The prothrombin time (PT) does not become abnormal until more than 80 percent of liver synthetic capacity is lost. This makes PT a relatively insensitive marker of liver dysfunction[26].

CONCLUSION

Progress of deterioration in level of different parameters of standard Liver Function Tests in a patient of chronic liver disease may alert clinician to the progress of liver damage. They can be considered by the clinician to evaluate the liver function again to determine status of liver function at that stage.

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Original Article

A Morphometeric Study of the Effects of Ibuprofen on the Stomach of Albino Rats under Light Microscope

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ABSTRACT

Objective: To observe the effects of ibuprofen on the stomach of the albino rats under light microscope and its morphometeric analysis.

Study Design: A prospective experimental study.

Place and Duration of Study: This study was conducted at the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi during 01.04.2008 to 31.05.2008.

Materials and Methods: Thirty male adult albino rats were taken for the study and were divided into two groups containing 15 animals each. Each group was divided in to three sub groups according to the time of sacrifice i.e. 4,6 and 8 weeks. Group A served as control. Group B received ibuprofen at the dose of 70 mg per kilogram body weight per day orally with feed. After completion of respective period of treatment animals were sacrificed, abdomen was opened. The stomach was removed and opened along the greater curvature, divided into cardiac, body and pyloric parts and was fixed in Buffered neutral formalin for 24 hours. After that tissues were processed in ascending strength of alcohol, cleared in xylene and infiltrated and embedded with paraffin. Five micron thick sections were made on the rotatory microtome, were stained with Haematoxylin and eosin (for general morphology and morphometric study), and with Periodic Acid Schiff Orange-G (for the mucus content of the surface mucus cells and the mucus neck cells), randomly selected every seventh stained section, in three fields were studied.

Results: In stained sections of all parts of stomach the lining epithelium was disrupted, exfoliated, and ulcers and erosions were present. The erosive areas contained red blood cells and extended deep in to lamina propria. The results of mucosal thickness and the mean values of number of surface mucous cell count was moderately significant ($P < 0.001$) to highly significant (($P < 0.0001$) in all parts of stomach when compared to control. The mucous content of the surface mucous cell in subgroups 'B'1, 'B'2 and 'B'3 of cardiac and pyloric parts were same marked (++++), while in body part of stomach it was moderate (+++) same as in control animals respectively.

Conclusion: Based on present study, it is concluded that Ibuprofen induces gastric mucosal damage.

Key Words: Ibuprofen. Hematoxylin and eosin, Periodic Acid Schiff Orange G

INTRODUCTION

Ibuprofen is the most commonly used NSAID. It was the first member of the Propionic acid class of NSAID to come into general use, (Gilman et al., 2006)[1]. Other Propionic acid derivatives include Ibuprofen, Naproxin, Fenoprofen, Ketoprofen, Flurbiprofen and Oxaprozin. These agents offer significant advantages over the aspirin and indomethacin because they are better tolerated as anti-inflammatory drugs (Kato, 2002; Hatazawa et al., 2006)[2].

It acts by inhibiting the enzyme cyclooxygenase (COX) which catalyzes the conversion of the arachidonic acid to prostaglandins. The first enzyme in the prostaglandin synthetic pathway is cyclooxygenase. This enzyme converts arachidonic acid to the unstable intermediates PPG2 and PGH2 and leads to the production of thromboxane A2 and a variety of prostaglandins (Gilman et al., 2006)[1]. The half life is roughly 2 hours. Propionic acid derivatives (Ibuprofen) are approved for use in the symptomatic treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, and acute gouty arthritis; they also are used as analgesics, for acute tendonitis and bursitis, and for primary dysmenorrhea (Gilman et al., 2006)[1]. Ibuprofen at doses of 200 mg and 400 mg is an efficacious, cost-effective, well-tolerated, single-ingredient, treatment of migraine. In addition ibuprofen provided a beneficial effect on associated symptoms of migraine including nausea, photophobia, phonophobia, and functional disability (Codispoti et al, 2001)[4]. Ibuprofen 200mg and 400mg is effective in reducing headache intensity and rendering patients pain-free for two hours. Photophobia and phonophobia improved with 400mg dosing (Suthisisang et al., 2007)[5]. The recommended dose of Ibuprofen is 600mg qid. It is equivalent to 4 grams of aspirin in anti-inflammatory effects (Katzung, 2004)[6] Ibuprofen enhances the effect of pyrazinamide during the initial phase of tuberculosis treatment in the mouse model (Byrne et al., 2007)[7].

It has been proved that non steroidal anti-inflammatory drugs like indomethacin and ibuprofen cause the topical mucosal injury and it is the critical factor in the, development of intestinal injury (Seager et al, 2000)[8].

Gastrointestinal adverse reactions from ibuprofen usage include mucosal ulcers and bleeding (Abraham et al., 2005)[9]. Ulcerations may range from small superficial erosions to full thickness perforations of muscularis mucosa. There may be single or multiple ulcerations accompanied by gradual blood loss leading to anemia or by life threatening hemorrhage (Maricic et al., 1999)[10]. Ibuprofen is most frequent cause of aseptic meningitis induced by drugs. (Rodriguez et al, 2006)[11]. Nitric oxide-linked ibuprofen can promote resistance to mucosal injury, possibly via local synthesis of Nitric oxide (Downing et al., 2005)[12]. Ibuprofen esterified with Nitric oxide abolished irritation and significantly reduced thinning of gastric mucosa (Dudkiewicz, 1981; Downing et al., 2005)[13]. Keeping above facts in mind the present study has was designed to observe the effects of the Ibuprofen on the gastric mucosa and evaluation of the histological changes under light microscope.

MATERIALS AND METHODS

This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute Jinnah Postgraduate Medical Center Karachi where 30 healthy and active adult albino rats of either sex between 90-120 days were selected for present study. The animals were divided into three groups, A, B and containing 15 animals each and were further sub-divided into three sub-groups containing 5 animals each according to time of sacrifice, i.e. 4, 6, and 8 weeks respectively. Group 'A' served as control. Group 'B' received ibuprofen (available in the market as "BRUFEN" by Bayer Laboratories, Karachi Pakistan) at the dose of 70 mg per kilogram body weight per day orally with feed (Dokmeci et al., 2007). The animals were sacrificed at the end of their respective period of treatment under the ether anaesthesia. Their abdomen was opened with a long midline incision. The stomach was removed and opened along the greater curvature with an incision extending from cardiac end to the pyloric end and the contents of the stomach were noted for color, consistency, and blood. The stomach was stretched, fixed and cleaned and dipped in normal saline very gently. The mucosa was observed grossly for color and hemorrhagic spots and then under dissecting microscope for color, blood vessels and hemorrhagic areas and the number of erosions/ulcers.

Stomach was divided into cardiac, body and pyloric parts and was fixed in Buffered neutral formalin for 24 hours. After that tissues were processed in ascending strength of alcohol, cleared in xylene and infiltrated and embedded with paraffin

Five micron thick sections were made on the rotatory microtome and were stained with Haematoxylin and eosin (for general morphology and morphometric study which was done under the light microscope under (8x ocular and 40x objective). Sections from body were also stained with Periodic Acid Schiff Orange-G (The mucus content of the surface mucus cells and the mucus neck cells was observed in all parts of stomach under (8x ocular and 40x objective), and was graded as follows: Mild (++) (secretions in the basal part of the cells). Moderate (+++) (secretions extending upto the middle part of the cells). Marked (++++) (secretions extending upto the apical part of the cells). The cardiac and pyloric parts were also stained with combined Alcian blue-Periodic Acid Schiff technique. Randomly selected every seventh stained section, in three fields were studied for morphology and morphometery. The statistical significance of difference of various quantitative changes between the groups was evaluated by student "t" test. The difference was regarded statistically significant if the 'P' value was equal to or less than 0.05. All calculations were done by utilizing computer software SPSS version 10.

RESULTS

GROUP-A: The animals of group 'A' were healthy and active. The external surface of the stomach was shinny and glistening and the internal surface was clearly identified into two parts the grayish white part (esophagus), and the pink part which was continuous with the duodenum.

Table No.1: Mean* value of Erosions / Ulcers recorded in the Stomach of Different Groups of Albino Rats

Groups	Sub-groups	Treatment Given	Erosions of ulcers recorded in Stomach		
			4th Week	6th Week	8th Week
A	A1	Control	0		
	A2			0	
	A3				0
B	B1	Ibuprofen	6±0.31		
	B2			6±0.63	
	B3				9±0.63

*Mean±SEM

In H&E stained sections the surface lining cells were composed of simple columnar epithelium with oval to round nuclei. The lamina propria of all parts of stomach consisted of glands, connective tissue fibers and few lymphocytes. The muscularis mucosae consisted of smooth muscle fibers. The sub mucosa consisted of loose connective tissues with few blood vessels. The muscularis externa of cardiac part consisted of smooth muscle fibers which were arranged as inner circular and outer longitudinal layers but in the body and pyloric part it consisted of inner circular, middle longitudinal and outer oblique layers. The serosa was visualized normal in appearance. In Alcian blue-PAS stained sections of cardiac and pyloric parts, the surface mucus cells were present on the luminal surface of the stomach

and the mucus neck cells showed normal histological architecture.

Table No.2: Mean* value Mucosal Thickness (µm) of different parts of Stomach in Different Groups of Albino Rats

Groups	Sub-groups	Treatment Given	Measurement thickness of cardiac part of stomach		
			4th Week	6th Week	8th Week
A	A1	Control	431.40±12.36		
	A2			416.60±2.655	
	A3				418.00±2.565
B	B1	Ibuprofen	375.80±2.28		
	B2			368.60±3.14	
	B3				368.86±2.276
Groups	Sub-groups	Treatment Given	Measurement thickness of body of stomach		
A	A1	Control	560.00±1.516		
	A2			566.00±1.816	
	A3				572.00±1.414
B	B1	Ibuprofen	446.00±1.549		
	B2			441.00±1.095	
	B3				431.00±2.701
Groups	Sub-groups	Treatment Given	Measurement thickness of pyloric part of stomach		
A	A1	Control	559.20±2.49		
	A2			579.60±1.63	
	A3				580.40±2.46
B	B1	Ibuprofen	548.20±2.10		
	B2			555.00±3.22	
	B3				544.60±2.03

*Mean±SEM

Table No.3: Mean* value of Mucus Cell Count in the Cardiac Part of the Stomach in Different Groups of Albino Rats

Groups	Sub-groups	Treatment Given	Mucus cell count in the cardiac end of stomach		
			4th Week	6th Week	8th Week
A	A1	Control	66.60±0.87		
	A2			66.60±1.695	
	A3				67.40±0.50
B	B1	Ibuprofen	55.20±1.31		
	B2			51.80±1.11	
	B3				48.60±1.16
Groups	Sub-groups	Treatment Given	Mucus cell count in the body part of stomach		
A	A1	Control	54.40±1.363		
	A2			56.60±0.927	
	A3				56.20±0.663
B	B1	Ibuprofen	45.20±1.392		
	B2			40.80±0.860	
	B3				45.60±1.503
Groups	Sub-groups	Treatment Given	Mucus cell count in the pyloric part of stomach		
A	A1	Control	65±0.83		
	A2			64.20±1.11	
	A3				63.60±0.50
B	B1	Ibuprofen	55.20±1.01		
	B2			54.20±0.73	
	B3				50.40±0.75

In the PAS orange-G stained sections of the body of stomach consisted of gastric glands. The mucus neck cells were cuboidal to columnar in shape, mostly located in the neck region of the gastric glands; these cells gave irregular appearance due to compression of surrounding cells. The parietal cells were large and oval

in shape located at the base of the glands, few of them were in the neck region, the nuclei were rounded and placed in the centre of the cells. The chief cells were present on the basal part of the gland, as mostly pyramidal in shape, the nuclei were oval in shape lying in the base of the cell, where as the apical region was clear and filled with vacuolated spaces. The mean values of number of erosions/ulcers of stomach are shown in table 1. The mean value of mucosal thickness is shown in table 2. The mean values of number of surface mucous cell count are shown in table 3.

GROUP-B: Animals of group 'B' were weak, and sluggish in activities. The gross observation of the external surface of stomach was dull, under the dissecting microscope the mucosa was red, swollen and erosions were observed in all subgroups.

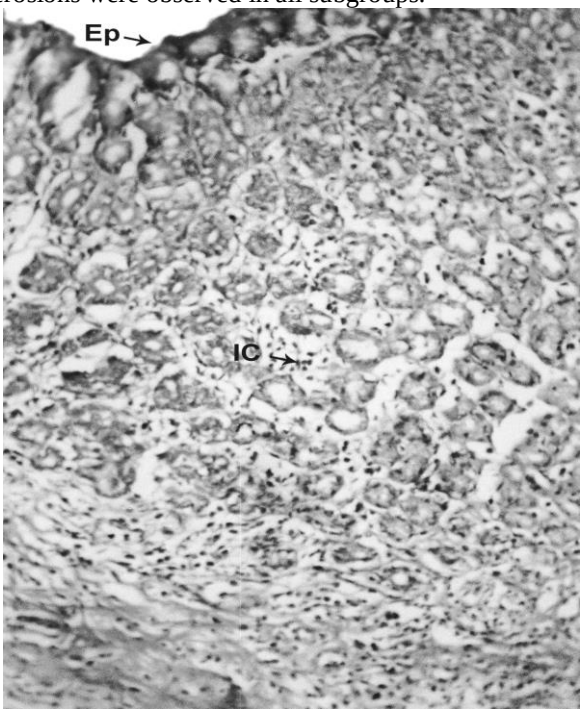

Figure No.1: H&E stained, 5µm thick sections of the body of the stomach in Ibuprofen treated albino rat, showing the (Ic) inflammatory cells in the lamina propria, (Photomicrograph x100). (6th week)

In H&E stained sections of all parts of stomach the lining epithelium was disrupted, exfoliated, and ulcers and erosions were present. The erosive areas contained red blood cells and extended deep in to lamina propria. The nuclei were small in size in between the eroded areas in subgroups 'B'1 and 'B'2. In subgroup 'B'3 the nuclei became pyknotic. The inflammatory cells were observed within and around the erosive areas, and in lamina propria. The erosions/ulcers were observed more in the pyloric part in subgroup 'B'3 while in cardiac and body parts the erosions/ ulcers were more in subgroups-'B'1 and 'B'2. The muscularis mucosae consisted of smooth muscle fibers arranged circularly in all subgroups. The submucosa showed normal appearance consisting of loose connective tissues with few blood vessels in subgroups 'B'1 and 'B'2. In subgroup 'B'3 the inflammatory cells extended in the submucosa. The muscularis externa in all subgroups consisted of two layers of smooth muscle fibers, inner circularly arranged and outer longitudinal.

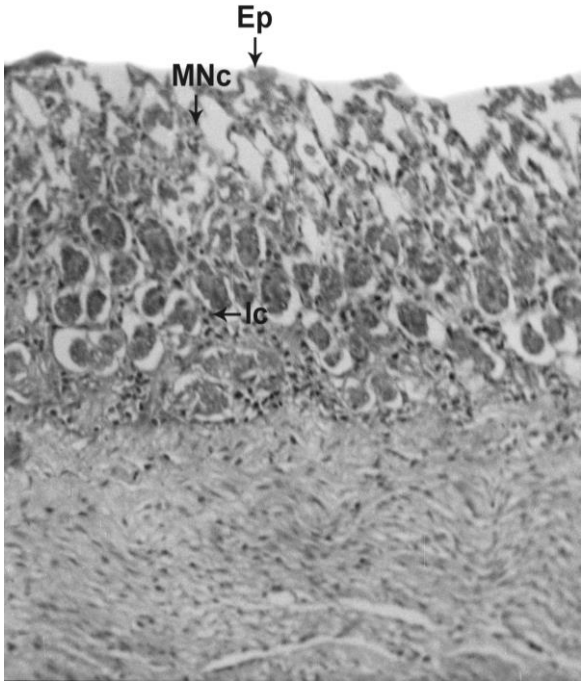

Figure No.2: Alcian blue-PAS stained, 5µm thick section of the pyloric part of the stomach in Ibuprofen treated albino rat showing the (Ep) disrupted epithelium, (MNc) distorted mucus neck cells and (Ic) inflammatory cells in the lamina propria. (Photomicrograph x100).(8th week)

The serosa was visualized as normal in appearance; connective tissue fibers and cells were loosely arranged. In Alcian blue-PAS stained sections of the cardiac and pyloric part the surface mucus cells were less in number and elongated in appearance, the gland cells were elongated and few. The cells were enucleated and nuclei were visualized in the lumen. The PAS orange-stained sections of the body of the stomach consisted of gastric glands. The mucous neck cells were distorted in shape and decreased in number. The parietal cells were more in number and small in size, their nuclei were present in the lumen of the gland. The chief cells were decreased in number, the shape was distorted, and the apical part of the cells was vacuolated. The nuclei were present in basal part of the cell. The mean values of number of erosions/ulcers of stomach are shown in table 1.

The mean value of mucosal thickness in cardiac parts of subgroups 'B'1, 'B'2 and 'B'3 the mucosal thickness was decreased in 'B'1 it was moderately significant ($P< 0.001$) while in 'B'2 and 'B'3 it was highly significant ($P<0.0001$) when compared with control. In body part

of stomach in subgroups 'B'1, 'B'2 and 'B'3 the mucosal thickness was decreased and was moderately significant (P< 0.001) when compared to control. In pyloric part in all subgroups the mucosal thickness was decreased and was moderately significant (P<0.001) when compared with control (Table 2).

The mean values of number of surface mucous cell count are shown in table 3. The number of mucous cell count was decreased in all sub groups of the cardiac part. The results were moderately significant (P<0.001) in subgroups 'B'1 and 'B'3 while highly significant (P< 0.0001) in 'B'2 when compared to control group. In the body part the surface mucous cells count was decreased in subgroup 'B'1, but was moderately significant (P<0.001), while in subgroups 'B'2 and 'B'3 the cells were decreased significantly (P<0.05) when compared to control groups. In pyloric part the number of mucous cell count was decreased in all subgroups. The results were moderately significant (P<0.001) in subgroups 'B'1 and 'B'3 while significant (P<0.05) in 'B'2 when compared to control group.

The mucous content of the surface mucous cell in subgroups 'B'1, 'B'2 and 'B'3 of cardiac and pyloric parts were same marked (++++), while in body part of stomach it was moderate (+++) same as in control animals respectively.

DISCUSSION

The present study was designed to observe the effects of on ibuprofen on the stomach of the albino rats. The animals treated with Ibuprofen in group-B appeared ill looking with loss in their body weight. Same findings were observed by the Dudkiewicz (1981)[14].

In the group-B animals, the number of ulcer was increased significantly the findings of presence of ulcers over gastric mucosal surface are in agreement with the findings of Tanaka (2002)[15] who used Indomethacin, Floribprofen, Naproxen, Kato (2002)[15] used indomethacin and rofecixib; and Jimenez et al (2004)[16] used Ibuprofen in their experimental studies on rat and measured the size of lesion under dissecting microscope.

Sequential observations of the changes between 4 and 8 weeks post-treatment with Ibuprofen showed that desquamation of the surface epithelial occurs in 4 weeks, while more extensive disruption and exfoliation of the surface epithelium and ulceration appeared in 8th week. Takeuchi et al (1992)[17] reported that HCl-induced gastric injury in rats by histological examination the apparent damage in the surface epithelial cells and disruption of epithelial membrane. Kumar et al (2003)[18] reported that NSAIDs-induced gastric mucosal defects which varied in extend from the superficial mucosal lesion down to the entire thickness of mucosa.

In the present study the decrease in mucosal thickness in group-B could be attributed to the injury caused by Ibuprofen, which resulted in demolition phase at 4th week of treatment, at 6th week extensive exfoliation of the surface epithelial cells and at 8th week damage of mucosa was more extensive with surface ulceration. Depending on the severity of injury, the mucosal response varies from vasodilatation and edema of the lamina propria, to erosion and hemorrhage. Many of their effects are probably mediated by an inhibition of prostaglandin synthesis as suggested by Underwood (2004)[19]. Hung (2006)[20] observed that necrotic cell-injury was found in both epithelial layers and lamina propria when gastric juice was present in the stomach of rats with ischemic brain.

The surface mucous cell count was significantly decreased in group-B due to progressive deterioration of gastric mucosa with time. As observed by Bagshaw (1987)[21] in an experimental study of aspirin-induced chronic gastric ulceration in the rat.

The present study demonstrates the inflammatory infiltrate is slight to marked degree in ibuprofen treated animals which confirms to the observations of Jimenez et al (2002). However at some places noticeable exfoliation accompanied by increased inflammatory infiltration in subgroup-B3 was observed. The present study also showed vaso-congestion which was concurrently increased with the extent of damage. Similar observations were confirmed by previous investigators (Kumar et al., 2004)[18].

In the present study the changes occur in mucus cells as a reaction to injury by ibuprofen in group B morphology was changed from slight to marked degree. The mucus content was increased in between the eroded/necrosis areas in group B animals, these findings are confirmed by (Kumar et al., 2004)[18].

CONCLUSION

Based on present study, it is concluded that Ibuprofen induces gastric mucosal damage.

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Original Article

Knowledge, Attitude and Practices of Barbers about Hepatitis B and C and its Transmission in Larkana City, Pakistan

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ABSTRACT

Background: Blood borne diseases impose heavy burdens on national economies and individual families due to costs arising from acute and chronic morbidity and mortality. Globally, 2 billion people are infected with hepatitis B virus (HBV). An estimated 170 million persons are chronically infected with hepatitis C virus (HCV) and 3–4 million persons are newly infected each year.

Transmission of hepatitis B & C through infected needles, blades, etc. is well known. Barbers are the important parts of community, as almost every man needs at least monthly visit to barber for hair dressing or shaving. In Pakistan the prevalence of shaving by barbers is reported to be as high as 34%–49% of the male population and it is important to know how barbers perceive the risks in relation to prevention of transmission of hepatitis B &C

Objective: To assess the knowledge and attitude of barbers regarding HBV and HCV and find out practices among barbers which may be responsible for transmission of HBV and HCV.

Study Design: Cross-Sectional Study

Place and Duration of Study: This study was carried out in the Larkana city during the months of March 2010 to April 2012.

Material and methods: A list of the barbers was obtained from the union of barbers and sample was drawn from that sampling frame. There were 422 barbers shops in the city. For sampling purpose Larkana city was arbitrarily divided into five zones (East, West, Central, South & North) and then 10 shops randomly selected from each zone. There were 156 barbers available and eligible for interview. After informed verbal consent, 132 barbers agreed to participate in the study. Data was entered, analyzed by Statistical Program for Social Sciences (SPSS) version 13.

Results: A total 132 barbers were interviewed. The mean age of respondents was 28$\pm$ 10 years, mean years of experience in barbering was 12.7 $\pm$10. More than half (63.6%) respondents were married. Majority of the respondents (84.8%) were resident of urban areas. 64% barbers have had knowledge that hepatitis B & C can be transmitted through blood transfusion and sexual contact. Only 6.1% had been vaccinated against the hepatitis B. 70% of the barbers disposed of used blades in regular garbage. 82% washed hands before and after shaving each client, 92.4% cleaned their instruments with disinfectant after shaving the, 99.2% barbers change the blade for each client

Conclusion: The knowledge of barbers regarding the transmission of hepatitis B & C was fairly good but majority of the barbers were not vaccinated against Hepatitis B though they were knew that vaccine is available against the hepatitis B

Key Words: Barbers, Hepatitis B & C, Knowledge, Attitude. Practices.

INTRODUCTION

Hepatitis is an inflammation of the liver, most commonly caused by a viral infection. There are five main hepatitis viruses, referred to as types A, B, C, D and E. These five types are of greatest concern because of the burden of illness and death they cause and the potential for outbreaks and epidemic spread.[1]

Hepatitis A and E viruses are transmitted typically by oro-fecal route. Hepatitis B, C and D viruses are usually transmitted by parenteral route, which include receipt of contaminated blood or blood products, invasive medical procedures using contaminated equipment, any skin injury with contaminated object, and for hepatitis B transmission from mother to baby at birth (vertical transmission) and also by sexual contact.[2,3]

Globally over 2 billion people have been infected with hepatitis B virus (HBV) and an estimated 170 million people are chronically infected with hepatitis C virus (HCV) [4,5]. In Pakistan specific estimates for the prevalence of both diseases range from 2–10%[6,7]. Recently the rates of HBV infection in the country have been increasing, attributed to a lack of proper health facilities, low socioeconomic status and low public health awareness about the transmission of communicable diseases[8].

HBV is 50 to 100 times more infectious than HIV, yet is transmitted by contact with blood or body fluids of an

infected person in the same way as HIV [2]. Razor shaving by barbers has been identified as a key risk factor for transmission of HBV [7] and HCV [9,10]. In Turkey 39.8% of barbers were found to be HBV positive and many were infected during the course of employment.[11,12] HBV and HCV infections have been implicated as an occupational hazard of the barbers' trade in several developing countries[11–12]. In Pakistan, daily facial shaving and armpit shaving from barbers has been identified as a risk factor for transmission of HBV and HCV [13–14].

A very limited number of studies have been published in Pakistan regarding investigating knowledge, attitude and practices about hepatitis transmission among barbers[15]. Researcher therefore have designed the current study to assess the knowledge, attitudes and common practices of barbers in Larkana city, Sindh province regarding risk of transmission of HBV and HCV in their work. This information will help to guide the design and implementation of appropriate prevention and interventions strategies.

MATERIALS AND METHODS

This cross-sectional study was carried out during the months of march- April 2012 in the Larkana city, which is the fourth largest city in the north-western part of Sindh Province, with a total area of 17 km2, with population of 2.6 million (2009).[16] A list of the barbers was obtained from the union of barbers and sample was drawn from that sampling frame.

Sample technique: The target population of study was people working in the barber shops and practicing hair-cutting and shaving. There were 422 barbers shops in the city. For sampling purpose Larkana city was arbitrarily divided into five zones (East, West, Central, South & North) and then 10 shops randomly selected from each zone. From the selected 50 shops, there were 156 barbers available and eligible for interview. After informed verbal consent, 132 barbers agreed to participate in the study.

Data collection: This cross-sectional survey was conducted during the months of March – April 2012. Trained medical students of final year visited the selected barber's shops. Face – to – face interviews were conducted with the barbers who willing to participate in the study. One of the students, not involved in data collection, observed the barbers and assessed his instruments use practices with the clients.

The questionnaire collected data about personal characteristics such as age, education, marital status and area of residence. In the knowledge section different knowledge based questions such as different modes of transmission of hepatitis and risk of transmission of the disease due reusing of blades and razors, were asked. In the attitude section questions like media they use for information, their knowledge about the vaccination against the disease, their vaccination status and how many doses they have received. While considering the practices, barbers were observed for hand washing before each client, sterilization of instruments and reuse of blades. Check list was used to record all these observations.

Analysis: Data were entered and analyzed by using the SPSS version 14. Percentages and frequencies were calculated for categorical variables and means and standard deviations for continuous variables.

RESULTS

A total 132 barbers were interviewed; their demographic characteristics are shown in table 1. The mean age of respondents was 28± 10 years, mean years of experience in barbering was 12.7 ±10. Twenty eight percent (37) barbers were illiterate, 32% (43) completed their primary education, and 41% had education up to intermediate and only 11% completed their higher education. More than half (63.6%) respondents were married. Majority of the respondents (84.8%) were resident of urban areas.

Table No.1: Demographic characteristics of participating barbers

Mean age (years) 28± 10

Mean years of experience In barbering 12.7 ±10.

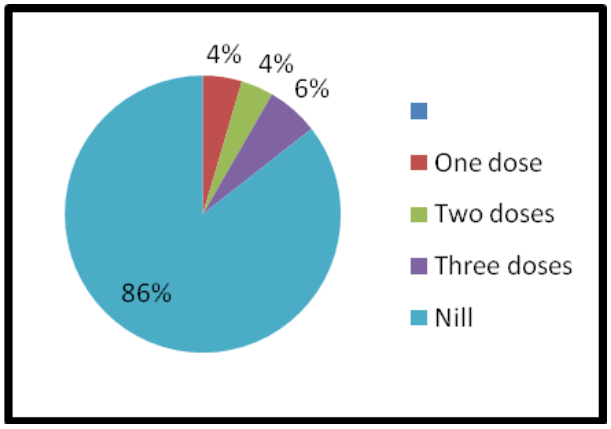
Educational status	**No**	**Percent**
Illiterate	37	29
Primary	43	32.6
Secondary	41	31.1
Higher	11	8.3
Residence		
Urban	112	84.8
Rural	20	15.2
Marital Status		
Married	84	63.6
Unmarried	48	36.4

Knowledge: Responses to the knowledge based questions showed that majority of the barbers (79.5%) were aware about the hepatitis B & C. Regarding the knowledge about the modes of transmission of the disease was good, 63% of the respondents knew about its transmission through barbers' instruments. About 64% barbers have had knowledge that hepatitis B & C can be transmitted through blood transfusion and sexual contact. Half (50%) of the respondents were knew that vaccine is available for the hepatitis B.

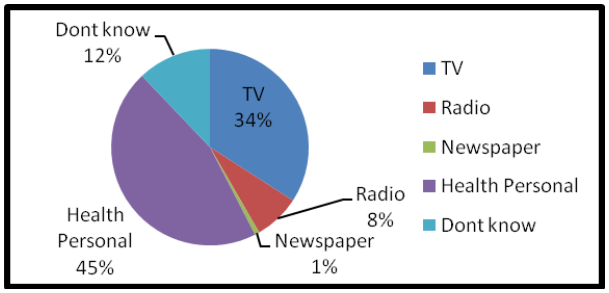
Attitude: The vaccination status of respondents was very poor, only 6.1% had been vaccinated against the hepatitis B. Main source of information regarding hepatitis B & C was health personal and TV (45.5% & 34% respectively), 70% of the barbers disposed of used blades in regular garbage.

Table No. 2: knowledge of the barbers regarding transmission of hepatitis B&C

Knowledge Item	Yes		No	
	No	%	No	%
General awareness				
Have heard about liver diseases	128	97	4	3
Have heard about HB&C virus	120	91	12	9
Mode of transmission				
Contaminated water	70	53	62	47
Contaminated food	81	61.4	51	38.6
Blood transfusion	84	63.7	48	36.3
Sexual contact	85	64.4	47	33.6
Reused needles	95	72	3.7	28
Barbers instruments	83	63	49	37
Vaccine available				
Against HBV	72	54.5	60	45.5
Against HCV	46	35	86	85

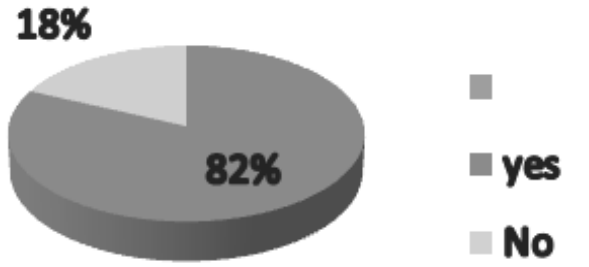


Graph No.1: Vaccination status of participants

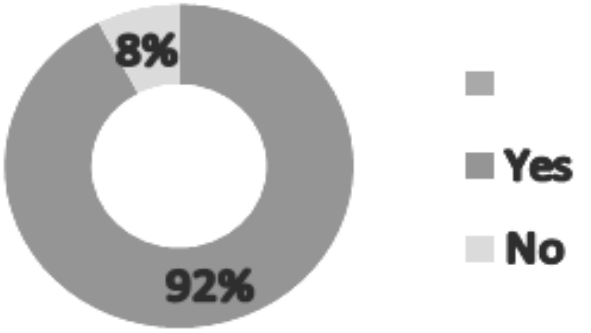


Graph No.2: Source of information

Practices: While observing the barber's practices, it was observed that 82% washed hands before and after shaving each client, 92.4% cleaned their instruments with disinfectant after shaving the, 99.2% barbers change the blade for each client



Graph No.3: Wash hands before and after each client



Graph No. 4: Disinfect instruments between clients

DISCUSSION

Barbers shop is the place where blade can act as a vehicle to transmit hepatitis B & C from one customer to another through sharing of blades between customers, which is common practice in Pakistani saloons. Moreover during rush period the chances of successful transmission of disease increase through reduction in the time between customers.[17,18]

This study was conducted to assess the knowledge, attitude and practices of the barbers about the transmission of the hepatitis B & C. The results show good awareness about the different modes of transmission of hepatitis B & C diseases. The majority of the participants were aware that disease can be transmitted through blood transfusion, sexual contact, reuse of needles and barbers instruments (63%, 64%, 72% and 70% respectively). This is better to another study conducted in Hyderabad Pakistan in 2007, which reported 29%, 36%, 31% and 36.6% respectively.[19] Knowledge about different modes of transmission of hepatitis in the barbers of Gharbia governorate, Egypt was better than our study which reported 94. 2%, 70.5%, 93.8 and 82.5% transmission of disease through blood transfusion, sexual contact, reuse of needles and barbers instruments respectively.[19]

In our study only one barber (0.8%) was observed to reuse the blade on different client compared to 4.3% of barbers of above mentioned study. Another study conducted in Turkey revels that 9.4% barbers were reusing the needles on different clients. In our study this may be because barbers were aware being observed

during data collection and majority of the barbers were not disposing the used blades in bins may have been intending reuse them later on.

Our study revealed that large proportion (85.6%) of barbers were ignorant regarding the vaccine against HBV only 6.1% barbers have had got all three doses of vaccine. The finding is in similar line with earlier reports.[20]

CONCLUSION

The present study was carried out in Larkana city to assess knowledge, attitude and practices regarding hepatitis B & C transmission in barbers. 132 barbers participated in study, selected randomly after dividing the city in to five arbitrarily zones.

A large proportion of the barbers were aware about the different modes of transmission of hepatitis B & C, particularly through blood transfusion, sexual contact reused needles and barbers instruments. While observing the practices of barbers, it was found that majority of the barbers washed their hands and instruments before and after each client. Although most of barbers were aware that vaccine against hepatitis B is available but only small number of barbers were fully vaccinated against the hepatitis B and there is a scope for educational intervention in this regard.

Recommendations:

At present, cure to HBV is a distant dream while treatment of HCV is available but it is very costly so the only cost effective measure is prevention as the only choice, through increasing awareness among people in general and particularly in people working in occupations where there is increased risk of transmission of HBV & HCV. Barbers occupation is probably one such occupation and has scope for educational intervention

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Original Article

Diagnostic Value of Fine Needle Aspiration Cytology in the Diagnosis of Solitary Thyroid Nodule

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ABSTRACT

Objectives:- To evaluate usefulness of the FNAC in diagnosing solitary thyroid nodule.

Study Design: Interventional study

Place and Duration of Study: This study was carried out in the Department of General Surgery, Nishtar Medical College, Multan from January 2010 to July 2010.

Material and methods:- A total of 100 patients were included in the study.

Results:- Majority of the patients i.e. 40 (66.7%) patients were between the 21-40 years. Of the 60 patients, 10 (16.7%) patients were male while 50 (83.3%) patients were female. Thirty five (58.3%) patients belonged to district Multan while 10 (16.7%) patients were residents of district Muzaffargarh. Mild pain was noted in 6 (10%) patients 3 (5%) patients had change in voice and 3 (5%) patients had palpitation. Thirty patients (50%) presented within one year of the start of their disease. Right lobe of the thyroid gland harboured swelling in 45 patients (75%). Only 3 patients (5%) were diagnosed as papillary carcinoma.

Conclusion:- Cold thyroid nodule is a common problem and has gained much significance due to its potential for malignancy.

Key Words:-FNAC, cost-effectiveness, thyroid nodules.

INTRODUCTION

Nodular thyroid disease is common and the incidence increases with age[1]. The prevalence rate is about 5% of the population[2]. Solitary thyroid nodule is a common presentation of thyroid swelling[3] and is more common in females. On scintiscanning, it may be cold, warm or hot. However, 75% of solitary nodules are cold[4]. This nodule may be adenomatous (hypertrophic or colloid), adenoma, localized area of Hashimoto's thyroiditis, cystic or in only 5% of the cases, the nodule is malignant[5].

Fine needle aspiration cytology (FNAC) is now recommended as the procedure of choice for evaluating all thyroid nodules. FNAC is not new. This technique was first used for cytological diagnosis of thyroid tumor in America in 1926. FNAC has been practiced over 80 years to diagnose infection and malignancy. FNAC is safe, simple, cost effective, time saving technique, requiring no anaesthesia, no danger of tumor dissemination and has excellent patient compliance[7,8]. FNAC has a high level of accuracy[9]. It is considered as the only preoperative diagnostic test that can often differentiate between benign and malignant nodules. So it helps in the operative planning of definite procedure based on cytology. Its only limitation is that it cannot differentiate between follicular adenoma and follicular carcinoma as this distinction is only made on histological criteria of capsular and vascular invasion. FNAC can also serve its therapeutic purpose in cystic nodules. This study will be done to evaluate the accuracy of the FNAC in the diagnosis of solitary thyroid nodule.

Thyroid diseases are quite common in southeast Punjab. Nearly all the disorders result in some swelling of the Thyroid gland and non-specific term "Goitre" embraces them all. In clinical practice, working classification is based on the biochemical status of the gland, physical characteristics of the gland and whether the gland is benign or malignant.

On physical examination, the swelling may be diffuse, multinodular or there may be a clinically discrete nodule. This discrete nodule is a common presentation of goitre and is more common in females. On scintiscanning, it may be cold, warm or hot. However, 80% of discrete nodules are cold[10]. This nodule may be adenomatous (hypertrophic or colloid), adenoma, localized area of Hashimoto's thyroiditis or carcinoma or may be cystic, in only 5-20% of the cases, the nodule is malignant[11].

This study was carried out to evaluate the usefulness of FNAC in diagnosing solitary thyroid nodule.

MATERIALS AND METHODS

This Interventional study was carried out in the Department of General Surgery, Nishtar Hospital, Multan from January 2010 to July 2010. A total of 100 patients were included in the study.

RESULTS

Out of 100 patients, 60 (60%) patients were between the 21-40 years, 20 (20%) patients in the age group 0-20 years and 20 (20%) were in the age group 41-60 years. Of the 100 patients, 15 (15%) patients were male while 85 (85%) patients were female. Most of the patients belonged to Multan. All the 60 patients (100%)

presented with swelling in front of neck. Fifty patients (50%) presented within one year of the start of their disease. Results are shown in following tables.

Table No.1: Site of lump

Site of lump	No. of patients	%age
Right lobe	75	75.0
Left lobe	25	25.0

Table No.2: Results of ultrasound

USG report	No. of patients	%age
Solid	75	75.0
Cystic	25	25.0

Table No.3: FNAC diagnosis

Cytology diagnosis	No. of patients	%age
hyroid cyst (Goitre with cystic degeneration)	10	10.0
Colloid nodule	50	50.0
Follicular neoplasm	15	15.0
Atypical cells	20	20.0
Papillary carcinoma	05	05.0

Table No.4: Surgical treatment (n=75)

Type of surgery	No. of patients	%age
Lobectomy	08	10.7
Lobectomy+ Isthmustectomy	40	53.3
STT	15	20.0
Near total thyroidectomy	12	16.0

DISCUSSION

Thyroid diseases are quite common in South East Punjab and present as a swelling in front of neck, which may be due to goitre, inflammation, cyst or malignancy. Thyroid nodules are fairly common surgical problems and the prevalence rate is about 5% of the population[12].

Thyroid diseases are quite common in South East Punjab and present as a swelling in front of neck, which may be due to goitre, inflammation, cyst or malignancy. Thyroid nodules are fairly common surgical problems and the prevalence rate is about 5% of the population[12].

Cold thyroid nodule has gained much importance because of increased potential for malignancy. The incidence of malignancy in cold nodules varies from 5 - 20% of the cases[13]. Because most of the clinically solitary thyroid nodules are cold, most cold nodules are benign and most malignancies are cold, they create a major surgical problem.

It has been demonstrated that up-to 44% of the clinically solitary nodules are, in fact, multinodular on ultrasonography and isotope scanning64. In the present study, 20 patients out of 60 (33.5%) having solitary nodules on physical examination were found to have multiple nodules on USG while thyroid isotope scan could detect multiple nodules in 7 patients (14%) due to the limited resolving capacity of the thyroid isotope scan. The isotope scan can resolve nodule, which is at least one cm in diameter[14].

Thyroid nodule occurs early in endemic areas[15]. In the present study, the peak incidence was between 20 -40 years of age. The nodules are more likely to be malignant at the extremes of age and in male sex[16]. In the present study, 4 of the 6 patients were the below the age of 30 years while 2 patient were above 50 years. Of the 7 male patients in this study, 2 had malignant nodule.

Out of 6 patients, having malignancy 2 patient (33.33%) had follicular carcinoma while 4 patients (66.66%) had papillary carcinoma, 2 patients were 55 years of age while 4 patients having papillary carcinoma were below the age of 30 years showing high incidence of papillary carcinoma in younger age group.

Right lobe of the thyroid gland is involved more often. In one study, right lobe was involved two times more than the left lobe[10]. In present study, 43 patients (86%) had nodules in right lobe while 7 patients (14%) had nodules in the left lobe.

Thyroid scan was extensively used in the past to divide the thyroid nodules into hot, warm and cold. The hot and warm nodules are rarely malignant while the cold nodules have 5 - 20% chances of malignancy. Thyroid scan is unable to distinguish benign nodules from malignant nodules[17]. In the present study, only 6 out of 50 cold nodules (12%) were malignant.

USG has the advantage of differentiating cystic from solid lesions and also the fact that it is non-invasive and free from radiation[17]. In one study, USG divided the cold lesions into solid, cystic or mixed with an accuracy of more than 90%[18]. In the present study, USG detected 15 lesions out of 50 (18%) as cystic. Eight of these 15 patients (55.55%) were subjected to surgery and the nodules were proved cystic and benign.

This ability of USG is limited by the fact that cystic lesions carry a significant risk of malignancy[19]. There are no definite criteria to discriminate benign and malignant lesions[20]. USG is useful in the follow-up of malignant tumours and benign nodules on LT4 therapy[21]. This incidence of carcinoma (27%) corresponds to the international figures by various authors[22].

In one study, diagnostic specificity of FNAC was 97.5% and diagnostic sensitivity and accuracy were 50% and 37.5% respectively. There were 1.4% false negative results while false positive results were found in 25%[23]. Cusick et al analyzed 283 patients undergoing FNAC and had specificity of 58% while sensitivity and accuracy of 76% and 69% respectively[24]. Anderson and Web in 1987, reported sensitively and specificity of 99.4% and 93.7% respectively[25]. The overall accuracy was 98.4%. They reported 6.3% false negative and 0.6% false positive results.

In present study, the diagnostic specificity has been calculated to be 90%. The diagnostic sensitivity and accuracy were 100% and 92 % respectively. False positive results were 8% and no false negative results were seen. This shows thyroid scan and USG only identify as group of patients with greater chances of malignancy while FNAC identifies cold nodule with definite or suspected malignancy with considerably high sensitivity. Because of its simplicity, excellent patient compliance and good histopathology correlation, the major use of FNAC is to reduce surgery and thus decrease morbidity in patients with benign nodules. The aim is satisfied if yield of malignancy goes up after investigations.

FNAC should be performed if thyroid nodules are clinically suspicious to be malignant (e.g. solid, rapidly growing)[26]. FNAC is now the gold standard and is widely used in the management of thyroid nodules[27]. It is cheap, minimally invasive and can be done under either palpation or ultrasound guidance. Its use has reduced the number of thyroidectomies by about 50%[28] and reduces the overall cost of medical care in these patients by 25%[29]. When properly done, FNAC should have a false negative rate of < 5% and false positive rate of about 1%[30]. Ultrasound guidance dramatically reduces sampling error and significantly improves sensitivity, specificity, as well as overall diagnostic accuracy[31,32]. FNAC cannot distinguish between follicular adenoma and follicular carcinoma.

CONCLUSION

FNAC represents a safe, cost effective and a reliable method of providing a tissue diagnosis and has become the first-choice investigations in the evaluation of solitary thyroid nodule, pre-operative diagnosis can be followed by better treatment strategy.

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Original Article

The Protective Role of Magnesium Sulphate on Steroid Induced Liver Damage in Albino Rats

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ABSTRACT

Objective: Dexamethasone causes metabolic disorders and morphological adverse effects on several organs of the body such as testes, kidney, bone, eye and liver etc. Most commonly it causes damage to liver morphology and its functions. Magnesium is an essential mineral of the body, currently is a subject of interest in medicine. Therefore the present study was designed to observe the ameliorating role of magnesium on dexamethasone induced liver damage and correlate the result with previous studies.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from 21 April to 10 May 2012.

Materials and Methods: Thirty adult albino rats, weighing from 200-300 grams were taken for this study. The rats were divided into 3 groups, Group A served as control , Group B received inj. dexamethasone 4mg/kg and Group C received inj. dexamethasone 4mg/kg with inj. Magnesium sulphate($MgSO_4$) 20mg/kg for 20days at the end of which they were sacrificed and liver tissue sections stained with haematoxylin and eosin.

Results: There was marked decrease in weight observed in rats receiving dexamethasone. Haematoxylin and eosin stained sections showed dilated central vein and sinusoids. Moderate fatty infiltration showed in vacuolated hepatocytes with absent or distorted nuclei in dexamethasone group which were protected and reverted to a major extent in Magnesium sulphate along with dexamethasone receiving group.

Conclusion: This study has proved that use of Magnesium sulphate along with dexamethasone ameliorates dexamethasone induced damaging effects on liver.

Key Words: dexamethasone, fatty infiltration, magnesium sulphate.

INTRODUCTION

In this era of science, we are standing on the verge of a revolution in medicine, understanding and treatment. The use of extensive drug coverage for treatment or saving life is increasing day by day, regardless of what side effects may occur on other organs.[1]

With all being said, steroids are life saving drugs and recommended in prudent quantities and dosages to save lives. However, these life saving drugs are not free from side effects. Prescribing steroids can be life-saving; however, this treatment can cause considerable hazards. The numerous complications, both major and minor, depend on its dosage & duration of treatment.[2, 3]

Glucocorticoids (GCs) are the major steroid hormones secreted by the adrenal gland. In therapeutics GCs are strongly immunosuppressive and anti-inflammatory; this has made this drug one of the most frequently prescribed drug worldwide.[4, 5]

Excessive glucocorticoids can have deleterious consequences, including increased risk of metabolic syndrome, which may lead to hyperlipidemia, hypertension, impotency, hyperlipidemia, amenorrhea, impaired liver function, and immune suppression.[6-8] Glucocorticoids can also have adverse morphological effects on several organs of the body such as testes, liver, kidney, bone, and eye etc.[9-14]

Dexamethasone, a synthetic glucocorticoid, increases both fatty acid and cholesterol synthesis. Cortisol leads to development of the visceral obesity and its pathologies. Short term effect of dexamethasone, a synthetic cortisol has been on both fatty acid and cholesterol metabolism in rat hepatocytes.[15]

Fatty change or steatosis refers to abnormal accumulation of lipids, mainly triglycerides in liver, since this is the major organ involved in metabolism. Steatosis is relatively benign and reversible. However, with a secondary cellular stress, such as the oxidative stress it may progress to steatohepatitis (NASH), which is characterized by necroinflammation and fibrosis.[16-19]

Since last year, biological role and properties of metal ions have been reconsidered due to greater importance of inorganic bio ions in explanation of numerous biologic processes. Magnesium is an essential mineral of the body. Accumulating evidence suggests that magnesium deficiency is associated with poor metabolic control and plays a key role in pathophysiology of insulin resistance, hypertension, increased cholesterol level in the body, and increased free radical dependent oxidative stress.[21]

Hypomagnesaemia might be a risk factor in the progression of fatty liver to steatohepatitis. Several studies confirmed the hepato-protective role of Magnesium.[22-25]

In the light of above mentioned background, and since no histological study has been done so far to assess the protective role of Magnesium on dexamethasone treated liver, this study was designed to observe the effects of magnesium against dexamethasone induce liver damage..

MATERIALS AND METHODS

This experimental study was conducted in the Department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, for 20 days from 21 April to 10 May 2012.

Thirty healthy, adult young male Albino rats, 90-120 days of age, weighing 200-300gm were taken for this experimental study. The animals were kept under observation for 1 week for the assessment of their health status and diet intake prior to the commencement of the study. After one week they were treated with injection Decadron (OBS pharma), 4 mg/kg[26] and injection magnesium sulphate (Zafa pharma), 20 mg/kg[27], according to experimental dose.

The experimental animals were divided into 3 main groups A, B, and C.

- Group A: animals served as control.
- Group B: were given injection dexamethasone intraperitoneal (IP) daily.
- Group C: were given injection dexamethasone intraperitoneal (IP) along with injection magnesium sulphate ($MgSO_4$) intramuscularly (IM) daily.

The animals were weighed and kept in cages, with twelve hour light and dark cycle under laboratory environment. All the animals were kept on standard laboratory diet and water ad libitum. They were sacrificed at the end of their treatment period. A midline longitudinal incision was given & after carefully exposing abdominal viscera; gross appearance of liver was noted. Liver was removed from the abdominal cavity and weighed. Liver was cut into two halves from the plane dividing into right and left lobes. Then both halves were fixed in the buffer normal saline (BNF) for 24 hours. Then tissue was processed by dehydrating through ascending grades of alcohol (70%, 80%, 90% and two changes 100%) and cleared in two changes of xylene. Tissues were embedded in tissue embedding system at 58 degree centigrade. 4 micron thick sections were made on glass slides and stained with Haematoxylin & Eosin. The stained slides were studied at 40 X objectives of light microscope and results were observed. The results were analyzed by student "t" test.

RESULTS

Over the course of treatment, dexamethasone administration in group B resulted in rapid and significant loss of body weight in comparison with control group A (P<0.0001). The group C protected by Magnesium sulphate showed minimal weight loss, & significant restoration of final body weight was noticed in this group in comparison with group B (P<0.001) (Table-1).

Inversely to the body weight, group B showed significant increase in mean liver weight (P<0.0001), which is significantly protected by the effect of Magnesium sulphate in Group C (P<0.001) and showed minimal or slightly increase in liver weight. (Table-2)

Microscopic examination of H& E stained section of control animals (Group A) showed normal architecture of liver, composed of hepatic cords which were radiating from the central vein; separated from each other by blood sinusoids. The hepatic lobules appeared almost hexagonal in shape (fig-1). Polygonal hepatocytes appeared normal with eosinophilic cytoplasm and centrally placed rounded nuclei with 1-2 nucleoli. Blood vessels & Periportal areas were seen normal (fig-2).

Dexamethasone treated (Group B) tissue sections showed disrupted lobular architecture with dilated and congested sinusoids. Focal necrosis of hepatocytes was seen. Hepatocytes were swollen & vacuolated. Nuclei had become pyknotic and fragmented. Cytoplasm appeared vesicular. Blood vessels were congested and dilated (fig-3). Portal areas were distorted and dilated along with lymphocytic infiltration (fig-4).

Table No. 1: *Mean body weight in different groups of albino rats at variable time interval

Groups	Initial wt. (gm)	End of 10 days (gm)	End of 20 days (gm)
A (n=10)	233.6±1.86	246.4± 3.86	244.8±3.67
B (n=10)	247.2 ±3.59	215.0±5.00	208.8±2.43
C (n=10)	234.0±4.35	234.9±2.67	221.9±1.45

*Mean±SEM

Statistical analysis of differences in the mean body weight between different groups

Groups	End of 10 days P-value	End of 20 days P-value
A vs. **B**	<0.001***	<0.0001****
B vs. **C**	<0.001***	<0.005**

Non-significant * Significant**
Moderately-significant*** Highly-significant****

Table No.2: Mean absolute weight of liver in different groups of albino rats

Groups	Mean liver weight (gm)
A (n=10)	6.100± 0.218
B (n=10)	10.594±0.405
C (n=10)	7.336±0.301

*Mean±SEM

Statistical analysis of Mean absolute weight of liver between different groups

Groups	P-value
A vs. **B**	<0.0001****
B vs. **C**	<0.001***

Non-significant * Significant**

Moderately-significant*** Highly-significant****

Magnesium sulphate protected (Group C) liver sections showed preservation of lobular architecture. Hepatic sinusoids were slightly dilated but not congested (fig-5). Hepatocytes appeared less vacuolated. Blood vessels were slightly dilated. Portal areas appeared almost normal (fig-6).

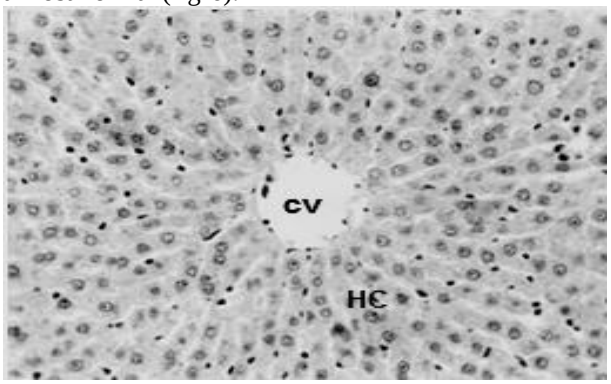

Figure No. 1: Photomicrograph showing normal hepatic architecture with central vein CV, hepatic cords HC, sinusoids and hepatocytes in control group-A under 40 X magnification

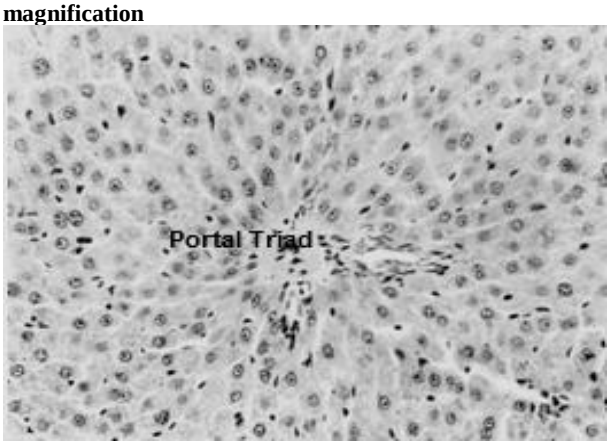

Figure No. 2: Photomicrograph showing normal hepatic architecture with, Portal Triad in control group-A under 40 X magnification

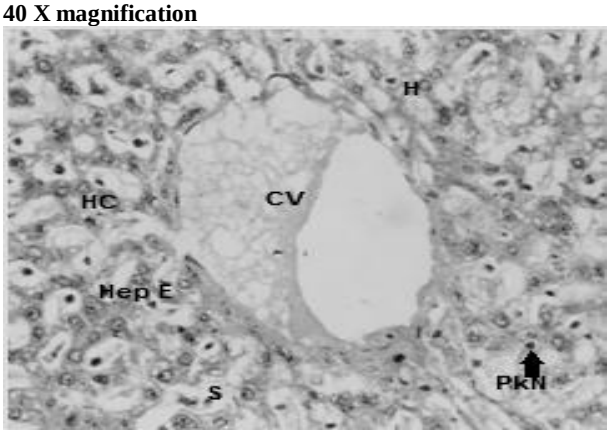

Figure No. 3: Photomicrograph showing empty, vacuolated hepatocytes Hep E, around a dilated and distorted portal triad , in dexamethasone treated group-B under 40 X magnification.

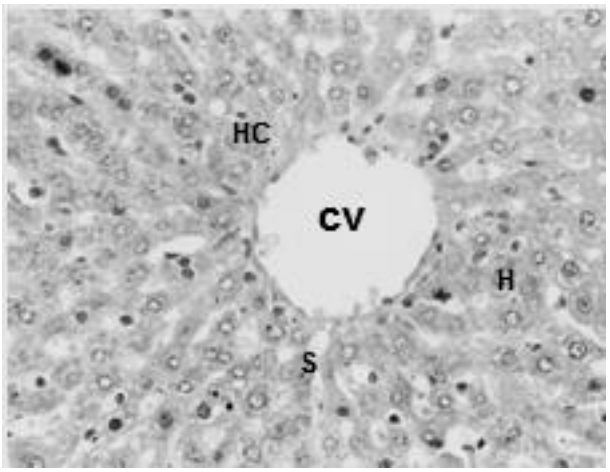

Figure No. 5: Photomicrograph showing preserved hepatic architecture with less dilated Central vein CV, regular arrangement of hepatocytes H, in hepatic cords HC, with slightly congested sinusoid magnesium protected group-C under 40 X magnification

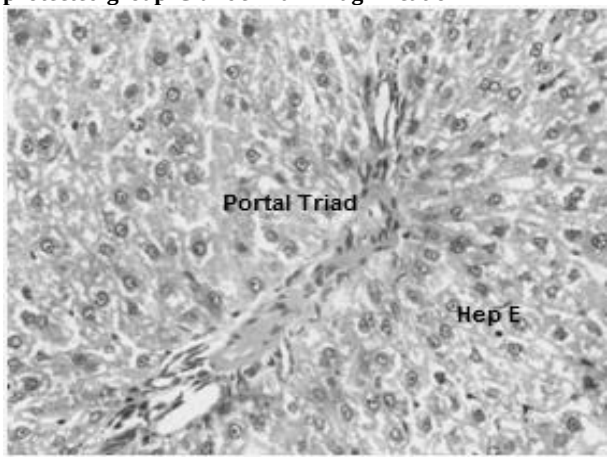

Figure No. 6: Photomicrograph showing preserved dilated Portal Triad and normal hepatocytes arranged in hepatic cords. Less empty & vacuolated hepatocytes Hep E were seen in Magnesium protected group-C under 40X magnification

DISCUSSION

Administration of dexamethasone has been reported to induce weight loss, insulin resistance, vascular disruption, altered lipid metabolism and fatty change in organs in several studies. Hepatic steatosis is very common finding in clinical practice.[8]

Magnesium is an obligate ion that is essential for activation of many enzymes involved in different metabolisms and functions, such as glucose metabolism, fatty acid synthesis and breakdown and DNA protein metabolism. [25]

In the present study, marked decrease in body weight was seen in dexamethasone treated animals (Group B) in comparison to control and Magnesium protected animals (Group C), this result is in accordance with Shafagoj et al. (2008)[8] who also observed decrease in

body weight in response to dexamethasone in albino rats.

There was a significant increase in liver weight in dexamethasone treated group-B, with grossly pale appearance of liver & signs of hemorrhage and congestion. This is in accordance to Micuda et al. (2007)[5] who also found increase in liver weight due to dexamethasone treatment, inversely to body weight of animals.

In the present study dexamethasone had disrupted the liver cytoarchitecture. It increased fat accumulation in the liver, which induced severe microvesicular steatosis with large vacuolated hepatocytes. This finding is in accordance to Matsunaga et al. (2008)[14] who also observed the vacuolation in liver cells due to dexamethasone administration. The central vein was congested and dilated. Sinusoids were dilated and leucocytic infiltration was seen. Similar findings were reported by Chaweeborisuit et al. (2009)[13].

This study also showed that Magnesium significantly ameliorated the effects of dexamethasone induced hepatic injury. Magnesium markedly improved the cytoarchitecture of liver. These findings are in agreement to Bao et al. (2008)[22] who also observed that magnesium reduced steatosis and relieved the congestion and dilatation of central vein and sinusoids

CONCLUSION

The present study concluded that dexamethasone causes moderate to severe hepatic damage and magnesium ameliorates the effects of dexamethasone on liver. Therefore it is suggested to avoid the irrelevant & long term use of dexamethasone and the concomitant use of magnesium prevents as well as reverts the liver damage.

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Original Article

Histological Study of Preventive Role of Cyanacobalamin (Vitamin B-12) On Heat Induced Testicular Injury

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ABSTRACT

Objective: The purpose of this study was to investigate the possible role of Cyanacobalamin (Vitamin B-12) in reducing the hazardous effects of heat on seminiferous tubules of testes in albino rats.

Study Design: Experimental Study

Place and Duration of Study: This study was conducted in the Department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, for 6 weeks from October 2010 to November 2010.

Materials and Methods: Thirty adult albino rats of 200-250 grams of weight and 90-120 days of age were taken for this study. They were divided into three groups A (control), B (heat treated), and C (heat plus Cyanocobalamin treated). They were further subdivided into A1&A2, B1&B2 and C1&C2, based on duration of treatment of 4 weeks and 6 weeks respectfully. At the end of study histological examination of seminiferous tubules of testes were seen by applying Periodic Acid Schiff Iron Hematoxylin stain.

Results: There was marked damaging effects of heat (42^0C) on seminiferous tubules of testes with disorganized germinal epithelium and vacuolation. This damage to spermatogenic cell series was well protected with concomitant treatment with Cyanacobalamin (vitamin B-12). There was restoration of germinal epithelium and marked decrease in vacuolation.

Conclusion: This study proved protective role of Cyanacobalmin (Vitamin B-12) in heat induced damage in testes of albino rats.

Key Words: Heat, Cyanacobalamin (Vitamin B-12), Testes

INTRODUCTION

Heat is the sensation of an increase in temperature or the energy which produces the sensation of heat[1]. Heat injury is an acute life-threatening situation when core temperature rises above 41°C[2]. Both excess heat and excess cold are important causes of injury. Prolonged exposure to elevated ambient temperatures can result in heat cramps, heat exhaustion, and heat stroke[3,4].

Various types of testicular injuries, including hormonal perturbations, heat exposure[5], Sertoli cell toxicants such as Tacrolimus, an immunosuppressant,[6] and germ cell toxicants like x-radiation,[7] immobilization stress,[8] alcohol,[9] Cadmium,[10] fungicides such as Mancozeb,[11] all result in germ cell apoptosis. Heat is produced by cellular metabolism, and lost through the skin by both vasodilatation and sweating and through the lungs in expired air. In health, the body core temperature is maintained at 37°C by the hypothalamic thermoregulatory center.[2] Studies in cell lines and animal models suggest that heat directly causes tissue injury.[12,13] Increasing testicular temperature above normal levels results in altered spermatogenesis in mammals due to effect of heat,[14] which brings about oxidative stress on the seminiferous tubules.

The effects of Cyanacobalamin (Vitamin B-12) deficiency is most pronounced in rapidly dividing cells, such as the erythropoietic tissue of bone marrow and the mucosal cells of the intestine.[15] Vitamin B-12 is important in cellular replication, especially for synthesis of RNA and DNA and deficiency states have been associated with decreased sperm count and motility.[16,17,18,19]. Vitamin B-12 (1000mcg/day) was administered to men with a sperm counts less than 20 million/ml. By the end of the study, 27 percent of the men had a sperm count over 100 million/ml.[20]

Several studies have been done on testicular tissue injuries by various agents such as heat, drugs, and radiations along with protective role of anti-oxidants like vitamin A, vitamin E and Selenium, but the role of vitamin B12 has not been explored in histological studies, so this study was planned.

MATERIALS AND METHODS

This experimental study was conducted in the department of Anatomy, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, for 6 weeks from October 2010 to November 2010.

Thirty (30) young male albino rats about 90-120 days of age and 200-220 gm of weight were obtained from animal house of BMSI, JPMC, Karachi.

Animals were divided into three groups A, B, and C. Each group was further subdivided into two subgroups, A1, A2; B1, B2; and C1, C2; based on the duration of treatment i.e. 4, and 6 weeks respectively. Each subgroup comprised of five animals.

The animals were kept under observation for one week, prior to the commencement of study for assessment of their health status. The animals were kept in plastic cages and were maintained on 12 hours light and 12 hours dark cycle. The standard laboratory chow and tap water were available ad libitum.

- Group-A (A1& A2) animals served as control.
- Group-B (B1&B2) animals had received heat at 42ºC for six hours daily with electric room heater and maintained with room thermometer.
- Group-C (C1&C2) animals received heat as given in group B and injection Cyanacobalamin, at dose of 500 mcg/kg body weight[21] intraperitoneally. All the animals were observed daily for their physical activity and weighed weekly. They were sacrificed under deep ether anesthesia at the end of their respective period of treatment. A mid line incision was made up to scrotum and extended upwards to the thoracic region.

The testes were fixed in Bouin's fluid for 24 hours. After 24 hours each testis was cut longitudinally into two equal halves and again post fixed in fresh Bouin's fluid for next 24 hours. The tissues were kept in capsules and then washed in running water for 3 to 4 hours to remove excess fixative. After fixation, tissues were processed in ascending strengths of alcohol, infiltrated and embedded in paraffin. 4µm thick longitudinal sections were cut on rotatory microtome. Sections of tissues were floated on hot water bath at 42ºC and transferred on albumenized glass slides. The slides were placed on hot plate at 37ºC for 24 hours for fixation of tissues and stained with Periodic Acid Schiff Iron Hematoxylin Technique. The morphological examination was done under light microscope.

RESULTS

The morphological examination of Periodic Acid Schiff-Iron Hematoxylin stained 4µm thick sections of testes in control subgroups; A1& A2 revealed seminiferous tubules cut in various planes of section under the light microscope. The tubules were compact, regularly arranged with intact basement membrane. The germinal epithelium was regularly arranged in various stages of spermatogenesis and the lumen contained spermatozoa. Vacuoles were not visualized .The Leydig cells were seen in groups in interstitial spaces which surround the seminiferous tubules and the dispersed chromatin material was seen within the cells (Figure-1).

On morphological examination of testicular tissue in subgroup B-1(4 weeks heat treated) animals, the seminiferous tubules were slightly distant but regularly arranged with intact basement membrane. Germinal epithelium was disorganized and germ cells were less in number. Spermatogenic material was compact in most of the basal layer.

Vacuoles were visualized. Leydig cells were dispersed and reduced in number and chromatin material in some cells was compact and showed some pyknosis (Figure-2).

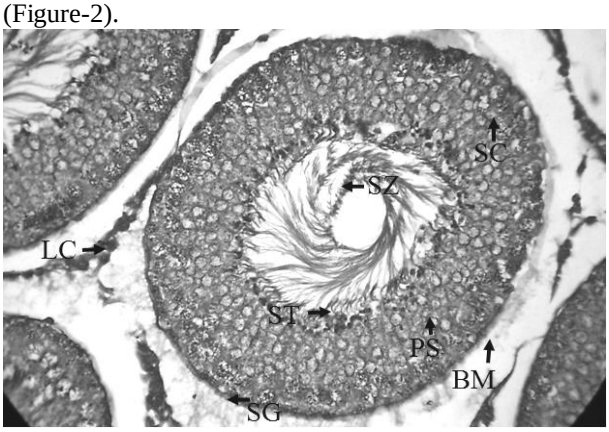

Figure No.1: PAS-Iron haematoxylin stained, 4 µm thick sections of testes of control albino rat, showing a seminiferous tubule with intact basement membrane (BM), spermatogonia (SG), primary spermatocytes (PS), spermatids (ST), sertoli cell (SC), lumen contained spermatozoa (SZ) and Leydig cells (LC) in the interstitial space. (Photomicrograph x40)

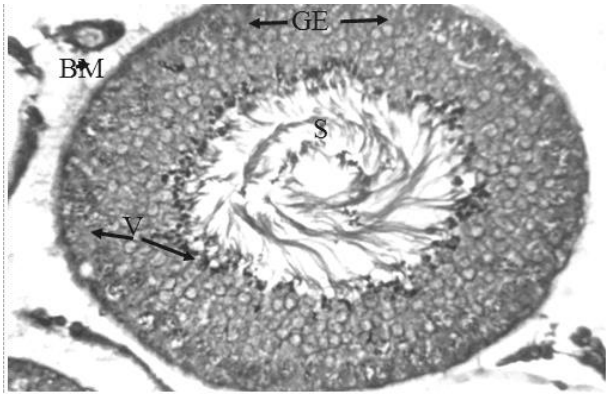

Figure No.2: PAS-Iron haematoxylin stained, 4 µm thick sections of seminiferous tubule, after 4 weeks heat treated showing disorganized germinal epithelium (GE) with more vacuolation (V), slough (S) but intact basement membrane (BM). (Photomicrograph x40)

The morphological examination of testes in subgroup B-2 (6 weeks heat treated) showed that the tubules were more widely separated as compared with B-I animals. There was shrinkage of seminiferous tubules. The germinal epithelium was scanty. Interstitial spaces were increased. Necrosis was seen at some sites. Compact chromatin in some tubules with pyknosis was seen. Slough was present in the lumen of most of the tubules. The Leydig cells were dispersed, less in number and reduced in size and nuclei showed pyknotic changes (Figure-3).

The morphological examination of seminiferous tubules in subgroup C-1 (4 weeks heat plus vitamin B12) showed the restoration of spermatogenic cell series similar to control. The basement membrane was intact

and vacuolation was remarkably decreased. Leydig cells were restored (Figure-1).

The morphological examination of seminiferous tubules in subgroup C-2 (6 weeks heat plus vitamin B12) revealed seminiferous tubules with slight widening of interstitial spaces, but basement membrane was intact. Lumen contained spermatozoa with some slough (Figure-4)

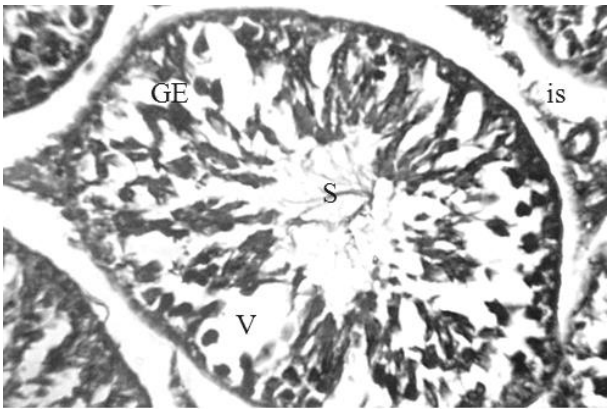

Figure No.3: PAS-Iron haematoxylin stained, 4 µm thick sections of seminiferous tubules, after 6 weeks heat treated showing scanty germinal epithelium (GE), widened interstitial space (IS), more vacuolation (V) and slough (S) in the lumen. (Photomicrograph x40)

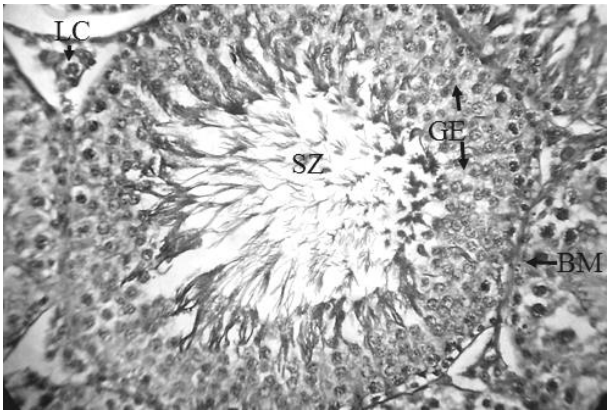

Figure No.4: PAS-Iron haematoxylin stained, 4 µm thick sections of seminiferous tubules, after 6 weeks heat with cyanacobalamin treated albino rats showing germinal epithelium (GE), with widening of interstitial spaces, intact basement membrane (BM), spermatozoa (SZ) in the lumen, and restored Leydig cells (LC). (Photomicrograph x40)

DISCUSSION

In the present study in heat treated group, the testes showed atrophy of seminiferous tubules, degeneration of germinal epithelium, specifically of spermatocytes and early spermatids producing vacuolation and slough. Kumar et al[3] described that persistent or excessive injury causes cells to pass the threshold into irreversible injury. This is associated with extensive damage to all cellular membranes, swelling of lysosomes, and vacuolization of mitochondria with reduced capacity to generate ATP. Yin et al[12] observed the effects of heat on testicular germ cells in adult mice with experimental cryptorchidism. They described the presence of vacuolation in the tubules representing sites of germ cells undergone apoptosis. Ren et al[22] showed degenerative changes (vacuoles) in experimental cryptorchidism in adult male rats. Impaired detoxification of reactive oxygen species and concomitant oxidative stress may be implicated in the biochemical mechanism responsible for testicular dysfunction in cryptorchidism.

Lue[23] reported that short exposure of the testis to heat causes degeneration of germ cells and apoptosis and germ cell death in the adult rat. A single exposure (43ºC for 15 minutes) of the rat testis to heat resulted in selective, but reversible, damage to the seminiferous epithelium through increased germ cell apoptosis[24,14] and mentioned that transient scrotal hyperthermia and Levonorgestrel enhanced testosterone-induced spermatogenesis suppression in men through increased germ cell apoptosis. The increased suppression of spermatogenesis is due to accelerated apoptosis mediated by the mitochondrial pathway of signaling. Apoptosis occurred mainly in the round spermatids and spermatocytes.

The animals in group C showed restoration of germinal epithelium, along with decrease in vacuolation. This could be the role of vitamin B12 in restoring serum testosterone levels and in reducing the oxidative stress. As B12 is reducing the stress, ACTH levels were decreased to near normal levels, resulting in might be near normal levels of LH which restored normal morphology of germinal epithelium. Courten and Ploen[25] in their study on adult cryptorchid testis observed that intratesticular infusion of Lactate showed improvement in various stages of spermatogenesis. Matsukiet al[26] in their study had noted that Minocycline decreased the effects of heat by decreasing the rate of apoptosis in mice testis. Yang et al[10] observed restoration of germinal epithelium by α-Tocopherol in Cadmium-induced testicular damage, by reduction of free radical damage and oxidative stress. The Leydig cells appeared smaller in size and their nuclei were darkly stained and some of them also showed pyknotic changes in heat treated animals as compared to control animals. The probable reasons for these changes may be hormonal disturbances and oxidative injury. As described by Norman[27], stress causes disruption of HP axis hormones. Lipid peroxidation due to oxidative stress of the cell membrane of Leydig cell causes reduction in the steroidogenesis[28]. The results of the present study are in agreement to Kanter and Aktas,[29] who also observed scrotal hyperthermia- induced damage in Leydig cells.

The Leydig cell arrangement was restored in group C animals. Their number increased and their nuclei were lighter stained as compared to heat treated group B

animals. The probable reason was due to the effects of vitamin B12 in decreasing stress so the ACTH levels are decreased and testosterone levels are increased to near normal. This increased level of testosterone helps is restoring the normal architecture of Leydig cells.

CONCLUSION

It is concluded that high ambient temperature severely damages the testicular tissue in albino rats, which becomes highly damaging with increased time period and can be protected by Cyanocobalamin.

It is suggested that, the results could be considered promising enough in humans who are working at high ambient temperature.

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Original Article

Rhomboid Flap in the Treatment of Pilonidal Sinus Disease

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ABSTRACT

Objective: The aim of our study was to present our experience with the Rhomboid flap technique in the management of pilonidal sinus disease and to evaluate the morbidity and recurrence.

Study Design: Cross-sectional, observational study.

Place and Duration of Study: This study was conducted in the surgical department of Nishtar Hospital Multan Ward 4 surgical unit I, October 2011 to March 2012.

Materials and Methods: Eleven patients were included, eight had previous surgical drainage of multiple natal cleft abscesses, and three had acute disease at the time of surgery. Nine patients had complex, recurrent pilonidal sinus. By using the Rhomboid transposition flap, we were able to excise the diseased area and close the defect. Operative time, hospital stay, healing time, wound infection, wound breakdown, return to normal activity and recurrence were assessed.

Results: There were 10 males and one female with a median age of 23 years (range 17–32 years). Mean follow-up was 6 months (range 5-6 months). Mean operative time was 63.2 minutes (range 55-75 minutes). Hospital stay was 3.4 days (range 2-5). Postoperative morbidity involved superficial wound infection in two patients, superficial gangrene of wound edges in one patient and partial wound breakdown in one patient that settled with dressing in the out-patient clinic. All wounds healed and the median healing time was 15 days. There was no recurrence in our series. Median time to return to normal activity was 17.8 (range 10-27) days.

Conclusion: Rhomboid flap is a useful technique in the treatment of advanced, difficult cases of pilonidal sinus disease. It has relatively low morbidity, allows early return to full activity and does not necessitate prolonged postoperative care. A larger series and longer follow up time is needed to assess the recurrence rate more adequately.

Key Words: Rhomboid flap technique, Pilonidal sinus disease.

INTRODUCTION

Pilonidal sinus disease is a painful and chronic condition affecting males predominantly and can lead to considerable discomfort and morbidity. It occurs in the intergluteal region and is the result of shed hair shafts through the skin, which ultimately leads to an acute or chronic infected site.**(1)**

In 1833, Mayo was the first to report a hair containing sinus and Hodges in 1880 suggested the term pilonidal sinus (Latin: *pilus* = hair and *nidus* = nest), to indicate a disease consisting of hair containing sinus in the sacrococcygeal area.**(2)** Buie**(3)** described the condition as jeep disease, because it is believed that it is caused by long periods of sitting in vehicles.

In 20% of cases, the disease is observed as an acute abscess, whereas in the remaining cases it presents as a chronic sinus, in which there are draining orifices.**(4,5)** Surgical drainage of pilonidal abscess can be used occasionally as a definitive treatment of small pilonidal sinus with abscess formation. However, advanced disease with multiple pilonidal sinus openings, branching tracts, and overt symptoms may require wide excision of the diseased region. The closure of the defect can be either by simple approximation of the edges or by using flaps.**(6)**

A simple excision and open wound healing cause more patient discomfort, longer hospitalization, require more time off work and requires regular outpatient dressing, whereas primary wound closure is associated with wound related complications, such as failure of primary wound healing and late pilonidal recurrence.

Thus, a large variety of flap techniques for covering the wound cavity were introduced.**(4,6–8)**

In this study we present our experience with one type of flap techniques for closure of the defect after excision of the pilonidal sinus, i.e. Rhomboid flap closure.

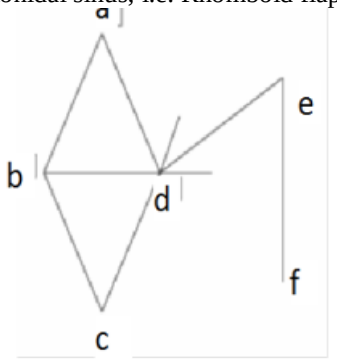

Figure No.1:

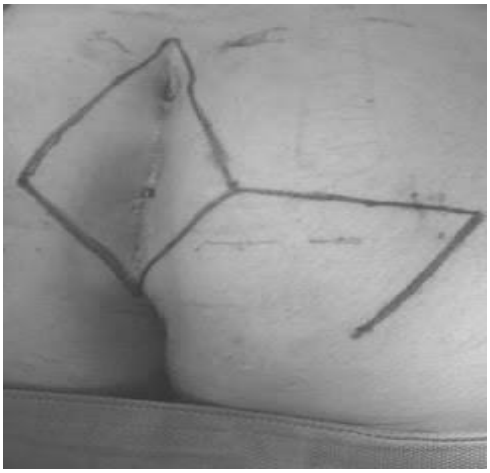

Figure No.2:

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Figure No.4:

Figure No.5:

MATERIALS AND METHODS

This study was conducted in surgical unit- I Nishtar Hospital Multan, from october 2011 to March 2012.. Eleven patients underwent the procedure. None of them had a sedentary life. Eight patients had previous multiple abscess formation requiring surgical drainage from their pilonidal disease and three had acute disease with pus discharge at the time of surgery. Nine patients had complex, recurrent pilonidal sinus. The procedure was explained to all patients and an informed consent obtained.

Preparation: All patients were admitted to the hospital one day before operation. All were operated on under general anaesthesia. A single dose of Ceftriaxone 1g was administered on induction of anaesthesia for prophylaxis against wound infection for all patients. were placed in the prone position, with buttocks strapped apart using adhesive bands. The sacrococcygeal area was shaved and cleaned using povidine-iodine. The extent of the sinuses was determined by inspection and palpation and all diseased areas were included in the incision.

Surgical Procedure: The area to be excised (abcd) is marked on the skin (Fig. 1) with the axis ac being along the natal cleft, with the anus below c. Lines cd and bd are then extended and the angle thus formed is bisected by lines having the same length as any one side of the rhomboid (thus ab =bc =cd =ad =de). Line ef is then drawn parallel to the long axis ac. The sinus (Fig. 2, 3) is excised down to the sacrococcygeal fascia centrally and the gluteal fascia laterally, and haemostasis is secured using diathermy. The rhomboid flap (Fig. 4,) is mobilized from the gluteal fascia and sutured without tension, with interrupted mattress sutures over a suction drain (Fig. 5). When there was an abscess, it was included with all diseased skin in the excised rhomboid.

Aftercare: After the operation, 500mg of Paracetamol and 50mg of Diclofenac Sodium were administered as soon as oral feeding was resumed for postoperative pain management for three days postoperatively. Patients were advised to lie on the lateral side until the wound healed. The dressing was changed on the second postoperative day, the drain is removed and the patients are usually discharged on the fourth day. The patients were advised on the importance of regular shaving of the buttocks and hygienic measures. The sutures were removed on the tenth postoperative day. Patients were followed up weekly for the first six weeks postoperatively, then monthly thereafter During each follow up session, bleeding, haematoma formation, infection, state of healing and recurrence were evaluated.

RESULTS

There were 10 males and one female with a mean age of 23 years (range 17–32 years). Clinical presentation included: local swelling (8 cases), pilonidal abscess (3 cases), and multiple sinuses with chronic suppurative discharge (9 cases) (see Table I). Mean operative time was 63.2 minutes (range 55-75 minutes). The duration of hospital stay was two to five days (mean 3.4 days). Primary healing occurred in nine patients when reviewed at the time of suture removal on the twelfth

day. One patient developed partial wound breakdown and one patient developed superficial gangrene of the wound edges, both were treated with dressings at the out-patient clinic. Postoperative complications were superficial wound infection in two patients, which needed daily dressing. All wounds healed, and the mean healing time was 15 days, range (12-21 days). None of the patients developed flap necrosis. Mean time to return to normal activity was 17.8 (range 10-27) days. Mean time off work was 21.4 days. Mean follow-up time was 6 months (range 5-6 months).

Table No.1: Clinical manifestations

Clinical manifestation	Patients	Frequency (%)
Local swelling	8	73
Acute abscess	3	27
Chronic suppurative discharge	9	81

Table No.2: Summary of results of different therapeutic procedures

Technique	Hospital stay (days)	Healing time (days)	Infection rate	Recurrence%
Phenol application[18]	0	-	-	8.3
Radiofrequency incision[25]	<1	42-75	0	0
Rhomboid flap[28]	3-10	14	0	7
Excision and marsupialization[23]	1.3	44.4	-	10
Excision and primary closure[35]	<1	12	2	6.3
Limberg flap[6,9,33]	5.6	-	0-23	4.7
V-Y flap[27,36]	3.5	-	0	0-5.9
Dufourmentel technique[13]	4	14	0	0
Present series	3.4	15	2	0

DISCUSSION

Pilonidal sinus disease occurs in the sacrococcygeal region. Hirsuteness, moderate obesity, puberty, vacuum effect and deep intergluteal sulcus are all factors that contribute to the development of the disease.[1,9,10] The incidence rate of pilonidal disease is approximately 700 per 100,000. The disease is found predominantly in whites; it is rare in blacks and practically nonexistent in Asians. It is now known that the pilonidal cyst is an acquired chronic disease of foreign body type caused by penetration of short, stiff hairs into the subcutaneous tissues.[2] Pilonidal sinus predominantly affects patients in their twenties and thirties and males more than females. In our series, age distribution was similar to that reported in the literature,[7,11,12] but with male predominance. Male to female ratio was 10:1 while some authors reported a male to female ratio of 1:2.[13] In this study, location of the pilonidal disease was in the natal cleft, nevertheless different locations for this condition have been described, including penis, axilla, perineal and suprapubic area, periumbilical zone, between the fingers of the hand (Barber's disease), and even in the ends of amputated extremities.[14,15] In spite of high incidence of pilonidal disease affecting young population and the prolonged disabling period caused by it, surgeons have not reached unanimity about the best treatment for this condition. Low recurrence rate, minimal inpatient stay, minimal cost, minimal operation time, minimal inconvenience, and minimal time off work are important considerations. Nonsurgical and surgical techniques were proposed. Nonsurgical techniques have included: local hygiene and weekly shaving of the sacrococcygeal area,[16] laser epilation of the intergluteal hair[17] and phenolization of the sinus tracts, but the later carries considerable risk of chemical burn and seroma formation.[18] Several surgical techniques have been described to date: cutting section,[19] cryosurgery,[20] aspiration followed by treatment with antibiotics, drainage with or without curettage,[9] excision and primary closure,[21,22] or excision and marsupialization,[23] vacuum assisted closure,[24] sinus excision and delayed closure.[25] Bascom *et al*.[26] reported that the most common cause of failure of healing after surgery is the deep cleft, moist and rolling action of the buttocks. Flattening the natal cleft was proposed to prevent the macerating action induced by rolling the buttocks while walking. Hence techniques which involved the obliteration of the deep natal cleft, such as Z-plasty[4] V-Y advancement flap,[27] rhomboid flaps[9,13,28] and primary skin grafting,[29] have been developed. Among these procedures, our treatment of choice is the rhomboid flap. We believe it is a very good plastic procedure for the treatment of pilonidal sinus however we try to use this technique only in cases of pilonidal sinus with multiple previous failed operations and when there is a large area which needs to be excised. A comparison of our results regarding hospital stay, healing time, infection rate and recurrence is similar to those reported in the literature (see Table II). Galala *et al*.[30] compared the rhomboid flap and the deep suturing techniques and showed higher healing rates and lower recurrence rate for the former. Our rates of healing and superficial wound infections are comparable to their findings. There is a high recurrence rate in most published series irrespective of the procedure.

Edwards[31] has reported a 46% recurrence rate for excision and healing by secondary intention and a 38% recurrence rate is quoted for excision and primary closure. Others[32] reported even higher recurrence rates

for those two techniques, whereas Manterola *et al.*[13] in a study on 25 cases that were treated by rhomboid flap technique, reported zero recurrence rate after a mean of 3.4 years of followup. Other studies[6,33,34] give a recurrence rate in the range of 2.5-4.8% for different periods of follow-up. We had no recurrence of the pilonidal sinus disease, but a longer follow up time will show the true results of this procedure. The reported average time lost from work was some 13 weeks of which 6–7 weeks were spent recovering from an operation designed to cure the condition.[28] In our study, the median time to return to normal activity was 17.8 days and off work time was 21.4 days. This is another advantage of this procedure, keeping in mind that more than 90% of our patients are working personnel.

CONCLUSION

Rhomboid flap is a technique used for the treatment of advanced, difficult cases of pilonidal sinus disease. The method is easy to use, has relatively low rate of wound infection, requires short wound healing time, does not need prolonged postoperative dressings, and allows early return to normal activities. A larger series and longer follow up is needed to give the true picture about the recurrence rates of pilonidal sinus following this procedure.

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Original Article

To Compare Lipid Changes in Glycemic Controlled Type 2 (NIDDM) and Glycemic Uncontroled Type 2 (NIDDM) Patients

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ABSTRACT

Background: Today diabetes is a global problem. Insulin play an inportant role in the lipid and lipoprotein metabolism. Glycemic control improves and may even normalize triglyceride and HDL cholesterol level in diabetic petients, therefore one could speculate the improvement of glycemic control beneficidly influence LDL phenolype. The degree of hyperglycemia was assesed by means of measmement of fasting blood glucose and glycosylated heamoglobin (Haemoglobin A_{1c}).

Objective: To compare the lipid profile in good glycemic controlled NIDDM type 2 with glycemic uncontrolled NIDDM type 2 and matched controls.

Study Design: Comparative study

Place and Duration of Study: This study was conducted at BMSI, JPMC, Karachi from June 2007 to December 2007.

Materials and Methods: Total 120 subject of either sex, age were included with set criteria in study and were distributed in to three groups. GroupA controls, GroupB glycemic controlled type 2 NIDDM using oral hypoglycemic drugs regularly – GroupC glycemic uncontrolled type 2 NIDDM using oral hypoglycemic drugs regularly. Lipid, lipoprotein and fasting serum sugar and HbA_{1C} were analyzed.

Result: Highly significantly increase in total chelestrol, triglycerides and LDL cholestrol, while significantly decrease in HDL cholestrol in glycemic uncontrolled type 2 NIDDM .

C**onclusion: F**asting serum glucose level and HbA_1c are useful diagnostic index for glycemic controlled and uncontrolled type 2 NIDDM – patient with glycemic uncontrolled type 2 NIDDM have greater disbances in lipid and lypoprotein metabolism which leads to atherosclerosis which futher results in coronary, cerebral and peripheral vascular occlusion

Key Words: Diabetes melltus Dyslipidemia, Glycosylated haemoglobin (HbA_{1c}).

INTRODUCTION

Today diabetes is a global problem. It is also anticipated that 75% of the world's diabetic population will be residing in developing countries. The rise is expected mostly in type 2 diabetes. In Pakistan 11.2% of people above the age of 25 years are suffering from diabetes mellitus [6] .Insulin plays an important role in the lipid and lipoprotein metabolism. Lipids and lipoprotein levels depend on the extent of insulin deficiency or insulin resistance, hyperglycemia, diet and the presence of concomitant primary and other secondary causes of hyperlipidemia [1]. While in current research, emphasis has been focused on qualitative abnormalities of plasma lipoproteins and alteration in their metabolism [5]. There is evidence of a close relationship between poor glycemic control and progression of dyslipidemia, most authorities aim for tight glycemic control especially in young patients [12]. Glycemic control improves and may even normalize triglyceride and HDL-cholesterol level in diabetic patients, therefore one could speculate that improvement of glycemic control beneficially influence LDL phenotype.[3] Intensive glycemic control does not necessarily mean multiple injection or insulin pump or have glucose monitoring 10 times a day. Intensive glycemic control means that the glycohaemoglobin, HbA_{1c} or blood glucose values are normal or near normal range, no matter how simple or how complex the treatment regimen [4].

The degree of hyperglycemia was assessed by means of measurements of fasting blood glucose and glycosylated haemoglobin (Haemoglobin A_{1c}) and integrated measure of long term blood glucose level that permits a more accurate assessment of "control" in non insulin dependent diabetic patients [21].

MATERIALS AND METHODS

120 subject were screened for this styudy. The subject were chosen from Diabetic Clinic Ward-7 JMPC, karachi and matched controls from healthy normal population. Previously diagonosed type 2 diabetes and non-diatetic subject having no history of renal, Liver , Thyroid Disease. Lactating women, persons who used lipid lowering drugs, cortricosteroids and estrogen drugs were not included in this study. The subjects were divided into three groups as non-diabetics (control)

group A, glycemic conrolled type 2 NIDDM group B, and glycemic uncontrolled type 2 NIDDM group C.

The subject were asked to come in the morning after an overnight fasting of at least 12-14 hours , about 10 ml of blood was taken from the anticubital vein , one ml of blood was saved in covered glass containing I mg/dl EDTA power, and was stored in a refrigerator at 2-8^{0}C, which was used for HbA1c estimation within 8 days Rest of blood was allowed to clot in the syringe. after 30 minuts serum was transferred from the clotted blood in the centrifuge tube.centrifugation was done for 10 minuts at 40 cycles per second.serum glucose was estimated on the same day by Enzyme calorimetic (GOD - PAP) methods, and rest of serum was presereved in plastic covered glass bottel at – 20^{o}C after proper labeling HBA1c was estimated by fast ion exchange resin separation method using kit (Clonital Cervico (BG) Italy), while serum triglyceride by Spinereact SA Spain. Moreover, LDL –Cholesterol was calculated according to Friedwalds formula.

RESULTS

Results of this study are summarized in tables 1 to 3. Total of 120 subjects, 80 Diabectic 40 non Diabetic healthy controls werer investigated during present study and were distrubuted into three groups. Table 1 shows the comparison of mean (±SEM) values of age, body mass index, systolic blood pressure and diastolic blood pressure in NIDDM patients with matched controls. Good Glycemic controlled NIDDM had a mean (±SEM) age of 53.50±1.35 years, body mass index 24.44±0.29 Kg/m^2, systolic blood pressure 116.75±2.36 Glycemic uncontrolled NIDDM had a mean (±SEM) age of 51.50±0.90 years, body mass index 23.30±0.45 Kg/m^2, systolic blood pressure 115.0±2.59 and pressuremmHg diastolic 72.25±2.36 mmHg.Control B had a mean (±SEM) age of 49.8±0.98 years, body mass index 22.70±0.34 Kg/m^2, systolic blood pressure 116.0±1.12 mmHg and diastolic blood pressure 76.25±1.39 mmHg.No significant difference of age, body mass index, systolic blood pressure and diastolic blood pressure were observed in Glycemic controlled and uncontrolled NIDDM patients with matched controls.

Table 2 shows the results of duration of disease, serum glucose and HbA_{1c} in glycemic controlled and uncontrolled patients of NIDDM with matched controls, no significant findings were observed in glycemic controlled as compared to controls.,while highly significant (P<0.001) in the levels of serum glucose and HbA_{1c} have been observed in glycemic uncontrolled NIDDM as compared to glycemic controlled NIDDM and matched controls. NIDDM. Table 3 shows the results of the total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol in glycemic controlled and uncontrolled patients of NIDDM with matched controls.

Table No.1: Comparison of Age, Body Mass Index, Systolic Blood Pressure, Diastolic Blood Pressure in NIDDM Patients with Matched Controls (All values are expressed in Mean±SEM)

Groups	Age (Years)	Body Mass Index (Kg/m^2)	Systolic (mmHg)	Diastolic (mmHg)
Group A Control	49.8± 0.98	22.70± 0.34	116.00± 1.12	76.25± 1.39
GroupB Glycemic controlled	53.50± 1.35	24.44± 0.29	116.75± 2.36	74.25± 1.96
Group C Glycemic uncontrolled	51.50± 0.90	23.30± 0.45	115.00± 2.59	72.25± 2.36

Table No.2: Comparison of Duration of Disease, Serum Glucose and HBA_{1c} In Glycemic Controlledand Uncontrolled Patients Of NIDDM With Matched Controls (All values are expressed in Mean±SEM)

Groups	Duration of Diabetes (Years)	Serum Glucose (mg/dl)	HBA_{1c} (%)
Group A Control	-	90.55±1.61	5.31±0.11
Group B Glycemic controlled	6.20±0.37	93.65±3.75	5.38±0.14
Group C Glycemic uncontrolled	6.05±0.37	*** 260.20±15.00	*** 9.56±0.25

*** (P<0.001) when compared to respective controls

Table No.3: Comparison of total Cholesterol, Triglyceride, HDL-Cholesterol, LDL-Cholesterol in Glycemic Controlled and Uncontrolled Patients of NIDDM With Matched Controls (All values are expressed in Mean±SEM)

Groups	Total Cholesterol (mg/dl)	Trigly-ceride (mg/dl)	HDL-Cholest erol (mg/dl)	LDL-Choles-terol (mg/dl)
Group A Control	165.10± 9.48	105.35± 7.38	47.35± 1.77	101.15± 9.82
GroupB Glycemic controlled	164.85± 8.64	104.65± 9.16	42.80± 2.39	101.20± 8.05
Group C Glycemic uncontrolled	***226.50 ±12.06	***192.45 ±10.63	***29.00 ±3.08	***159.10 ±12.49

*** (P<0.001) when compared to the respective controls.

Highly significant (P<0.001) increase in the level of total cholesterol, triglyceride and LDL-cholesterol, while highly significant (P<0.001) decrease in the level of HDL-cholesterol in glycemic uncontrolled NIDDM whereas, no significant change were observed in glycemic controlled NIDDM patients as compared to matched controls.

DISCUSSION

Diabetes mellitus predisposes to premature atherosclerosis due to dyslipidemia [10]. Accelerated atherosclerosis may be related to diabetic control as reflected by the degree of hyperglycemia and may in part be mediated by plasma lipid abnormalities. Patients with type 2 diabetes mellitus have twofold to fourfold excess risk of coronary artery disease (CAD) compared with non-diabetic patients. Indeed 75% to 80% of adult diabetic patients die of CAD [1316 17] . reported that their have been many abnormalities in blood lipids associated with diabetes mellitus because of obvious difference between IDDM and NIDDM. It is important to study these groups separately. They observed that increase in fasting plasma values of total cholesterol, triglyceride and LDL-cholesterol with increasing degree of hyperglycemia in IDDM as well as in NIDDM and also found reduction in plasma HDL-cholesterol concentration in glycemic uncontrolled IDDM and NIDDM patients. The results of present study were also in accordance with the findings of above observers as shown in table 3.

[25] . reported that to identify lipoprotein disorders, characteristics of diabetes, total cholesterol, triglyceride were determined in plasma in non obese NIDDM subjects who were classified into poorly controlled and well controlled groups based on the degree of glycemic control. They found that, in a well glycemic controlled, lipid disorders were no longer observed while in poorly glycemic controlled NIDDM, cholesterol, triglyceride were increased, because increased hyperglycemia lead to decreased LPL and LDL pathway activity induced under insufficient insulin action. Similar metabolic changes were noted in controlled and uncontrolled diabetes as shown in table 3. [13] . reported that low HDL-cholesterol and occasional LDL-cholesterol elevations commonly found in diabetic patients. For example, both the American Diabetes Association and the National Cholesterol Program recommended glycemic control as the first step in controlling diabetic dyslipidemia. There is no doubt that the principal modalities of glycemic control can improve lipid profile in selected diabetic patients. Thus diet, oral antidiabetic agents and insulin have all been shown to produce favorable changes in diabetic dyslipidemia as treated diabetics improved by lowering Triglyceride and LDL-cholesterol. [3 ,6 ,7 , 8.] Were agreed with this observation and further he observed that elevation of triglyceride also found in glycemic uncontrolled diabetes because the TG-HDL concentration is extremely complexed with numerous genes regulating the synthesis of apolipoproteins, lipids, enzymes, receptor and environment have major impact on lipoprotein metabolism. Present study has same trend as shown in tables 4 to 5. [11;14; 15;16; 17;18;21;22;23;24] reported that the most common lipid abnormalities seen in diabetic persons are elevated level of LDL-cholesterol, triglyceride and decreased HDL-cholesterol concentration in blood and these patients have preponderance of abnormalities in the composition of LDL-cholesterol is not significantly increased. In our present study, these observations also found in glycemic uncontrolled type 2 diabetics as shown in table 3.

CONCLUSION

Fasting serum glucose level and HbA_1c are useful diagnostic index for glycemic controlled and uncontrolled type 2 NIDDM – patient with glycemic uncontrolled type 2 NIDDM have greater disbances in lipid and lipoprotein metabolism which leads to atherosclerosis which futher results in coronary, cerebral and peripheral vascular occlusion.

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