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CONTENTS

Editorial Cardiac Problems -- The Stem Cell Approach

Dr. Azhar Masud Bhatti
Addl. Director Health Services, EPI Punjab, Lahore
&
Editor in Chief

While cardiovascular diseases can refer to many different types of heart or blood vessel problems, the term is often used to mean damage caused to your heart or blood vessels by atherosclerosis (ath-ur-o-skluh-Ro-sis), a buildup of fatty plaques in your arteries. This is a disease that affects your arteries. Arteries are blood vessels that carry oxygen and nutrients from your heart to the rest of your body. Healthy arteries are flexible and strong.

Over time, however, too much pressure in your arteries can make the walls thick and stiff sometimes restricting blood flow to your organs and tissues. This process is called arteriosclerosis, or hardening of the arteries. Atherosclerosis is the most common form of this disorder. Atherosclerosis is also the most common cause of cardiovascular disease, and it's often caused by an unhealthy diet, lack of exercise, being overweight and smoking. All of these are major risk factors for developing atherosclerosis and, in turn, cardiovascular disease.

Common causes of abnormal heart rhythms (arrhythmias), or conditions that can lead to arrhythmias include:

- Heart defects you're born with (congenital heart defects)
- Coronary artery disease
- High blood pressure
- Diabetes
- Smoking
- Excessive use of alcohol or caffeine
- Drug abuse
- Stress
- Some over-the-counter, medications, prescription medications, dietary supplements and herbal remedies
- Valvular heart disease

In a healthy person with a normal healthy heart, it's unlikely for a fatal arrhythmia to develop without some outside trigger, such as an electrical shock or the use of illegal drugs. That's primarily because a healthy person's heart is free from any abnormal conditions that cause an arrhythmia, such as an area of scarred tissue. However, in a heart that's diseased or deformed, the heart's electrical impulses may not properly start or travel through the heart, making arrhythmias more likely to develop.

Heart defects usually develop while a baby is still in the womb. About a month after conception, the heart begins to develop. It's at this point that heart defects can begin to form. Some medical conditions, medications and genes may play a role in causing heart defects. Heart defects can also develop in adults. As you age, your heart's structure can change, causing a heart defect.

There are many causes of diseases of your heart valves. Four valves within your heart keep blood flowing in the right direction. You may be born with valvular disease, or the valves may be damaged by such conditions as rheumatic fever, infections (infectious endocarditis), connective tissue disorders, and certain medications or radiation treatments for cancer.

The promise of stem cell therapy may have gotten a little closer to reality, with researchers reporting that they've used the cells to help shrink hearts that were dangerously swollen after heart attacks. The approach involves taking stem cells from a heart patient's own Bone Marrow, then injecting them into the patient's Damaged Heart. The result: a significant improvement of heart performance within months, and a significant reduction in both scar tissue and Heart size within a year after the initial therapy.

However, the study is small - a phase one clinical trial involving just eight male patients - and still described as "experimental." But the research team says that if confirmed in larger trials, the approach could be a big advance over current treatments for this type of Enlarged Heart. "The results are very encouraging," said study co-author Dr.Joshua M.Hare, a professor of Medicine and director of the Interdisciplinary Stem Cell Institute at the University of Miami Miller School of Medicine. The therapy has "been under development for about ten years, and finally now we are starting to take a big step forward," he said.

But Hare was also quick to note that much more research and time is needed before the novel treatment could become available to patients. "We can't say whether that'll be in three or seven years down the road. It's hard to speculate precisely. But we're talking sometime this decade," he said.

Hare and his colleagues discussed the findings in the March issue of Circulation Research.

According to the American Heart Association (AHA), Heart Enlargement can result from a number of health complications, including Heart attack, Congestive Heart failure, and a form of heart muscle inflammation known as Cardiomyopathy. Heart valve disease and High Blood Pressure can also contribute to Heart Enlargement as a result of heart muscle thickening.

Right now, according to the researchers, chronic use of medications and/or heart transplant are the only means of reducing the increased risk for death, disability, and

hospitalization that accompanies an enlarged heart. To test the new stem cell approach, the study team focused on eight men with an average age of 57. All had suffered a Heart Attack as far back as 11 years prior to their treatment.

Stem cells from Heart Attack patients helped improved blood pumping ability and restore vitality in cardiac muscle, according to a small trial published.

It is the first time patients have been given an infusion of their own cardiac stem cells in the aim of solving the impact of Heart Failure rather than simply treating the symptoms of it.

The findings are so promising that the study's chief investigator said a potential "Revolution" was in the offing if larger trials succeeded.

Stem cells are infant cells that developed into the specialized tissues of the body.

They have sparked great excitement as they offer hopes of rebuilding organs damaged by disease or accident.

The new study, published online in The Lancer, tested cardiac stem cells on 16 patients who had been left gravely ill as a result of an acute myocardial infection.

The index used for cardiac health is called the left ventricular ejection fraction (LVFV) which calculates the capacity of the left ventricle to expel blood in the space of a heart-beat.

For a person in normal health, the LVFV is 50 percent or higher.

Among the study patients, though, this had fallen to 40 percent or lower. At such a threshold, shortness of breath and fatigue are chronic and often disabling.

The stem cells were isolated from a coronary artery that had been removed when the patients underwent a coronary bypass.

Within four months of treatment, the LVFV rose by 8.5 percent and after a year by 12 percent, four times what the researchers had expected.

Original Article

Compare the Outcome of Open Versus Laparoscopic Varicocelectomy

1. Ubedullah Shaikh 2. Mujeeb Rehman Abbassi 3. Muhammad Sharif Awan 4. Muhammad Rafique Pathan

1. PG Student of Surgery, LUM&HS, Jamshoro 2. Asstt. Prof., Minimal Invasive Surgical Centre, LUM&HS, Jamshoro 3. Asstt. Prof. of Surgery, PUH, Nawabshah(SBA) 4. Sen. Registrar. of Surgery, LUM&HS, Jamshoro

ABSTRACT

Objective: To compare the outcome of the laparoscopic surgery with open varicocelectomy. It is also assess the operative time, postoperative pain, postoperative recovery of patients and postoperative complications of both procedures such as, bleeding, haematoma, wound infection, hyderocele , laparoscopic related complications and recurrence.

Study Design: Observational Study.

Place and Duration of Study: This study was carried out in Surgical Unit-IV, Liaquat University Hospital Jamshoro, from January 2009 to December 2010.

Materials and Methods: This study consisted of 80 patients of varicocele grade III were admitted and divided in two groups. Group A for open varicocelectomy and group B for laparoscopic varicocelectomy in which each group consist of 40 patients.

Results: The ages of patients ranged between 11 years to 50 years. The mean age of LV group was 25.72+6.026 years and for OV group was 27.58+6.694 years. In OV group 92.5% of patients were having left varicocele, 5% right varicocele and 2.5 bilateral disease where as in LV group 90% of cases were having left , 7.5 % right and 2.5% bilateral varicocele . The mean time in OV group was 29.70±8.498 minutes and 25.08±5.558 minutes in LV group (p 0.005). The mild pain was observed in 7 (17.5%) patients of OV group and 16 (40 %) patients of LV group. Whereas, severe pain was described by 10(25%) patients in OV group and 4 (10 %) patients in LV group (p 0.032).The wound infection was found in 6 (15%) patients of OV group and 2 (5%) patients of LV group . The hydrocele was seen in 5(12.5%) cases of OV as compared 2 (5%) cases of LV group. Residual varicocele and recurrence of varicocele was observed in two cases (2.5%) of OV group and 3 cases of LV group with value p <0.359. It was longer about 2-3 days in 34 (85%) of OV patients as compared to LV cases where majority 36(90%) were discharged within 1 to 2 days.

Conclusion: The results shows that LV is superior than OV in terms of better cosmesis, less operative time, less complications, short hospital stay and early return to work.

Key Words: Open Varicocelectomy (OV), Laparoscopic Varicocelectomy (LV), Complications of Varicocelectomy.

INTRODUCTION

Varicocele is a condition in which the veins of the pampiniform plexus are elongated and dilated. It is a common disorder in adolescents and young adults[1].This venus plexus bears the name "pampiniforms" because it wraps itself around the spermatic cords like a vine [2] .The incidence of varicocele in the general male population is 9 to 23% and increases to 40% in infertile patients[3] . It mostly occurs on left side 95% , both sides 11% and right side 4%[4] .

Varicosities develop due to mechanical problem in the drainage of the testicular veins primarily due to valvular incompetence at the level where they join with the main venous system on left side in left renal vein and on right side in inferior vena cava[2]. Thus, retrograde flow from any of these venous systems can also result in varicocele formation. Approach and techniques in the surgical treatment has remained debatable among surgeons. In principle, the treatment involves interruption of spermatic venous flow at any site along its course till its distal termination to stop the retrograde venous filling of these vessels. Thus the site of such an interruption may be scrotum, inguinal canal, low retroperitoneum or high retroperitoneum[5].In the study of Goulart TD [6] ,the inguinal open approach is more ancient and was first described by Ivannissevich in 1918 . The main advantages of claimed for retroperitoneal approach are simplicity and avoidance of injury to the testicular artery. Since last ten years minimal access surgical techniques shows significant advantages to open surgery, such as shorter hospitalization, reduced need of analgesic drugs, quick return to daily activities and better cosmetic results. Recently Laparoscopic Varicocelectomy is gaining popularity and is considered to be the treatment of choice in bilateral varicoceleotomy [7]

MATERIALS AND METHODS

This study was carried out in Surgical Unit-IV Department of surgery, Liaquat University Hospital Jamshoro, from January 2009 to December 2010. 80 patients of varicocele were admitted.

The patients were diagnosed by pre-operative workup and on clinical parameters and doppler ultrasound finding. The patients were divided into two groups, A for open and B for laparoscopic varicocelectomy each comprising of 40 patients. A detailed history and clinical examination, operative findings , postoperative recovery , postoperative complications and follow up record was made on especially designed proforma. Clinical examination of the patient was done with assessment of swelling in scrotum & palpable veins like bag of worms at the bottom of scrotum .

All patients underwent for base line investigations. The patients were consulted about their willingness and written consent before adapting either of the operative method i.e, Laparoscopic or open Varicocelectomy. All 80 patients with symptomatic varicocele or grade –III varicocele or varicocele were Included in the study irrespective of their age .Where as the patients unfit for general anesthesia; patients with grade I varicocele; patients who were asymptomatic having no effect on fertility; and the patients with other associate problems like inguinal hernia, atrophy of testis , orchitis were excluded from study. The follow up comprised mandatory 1st visit after one week for removal of stitches and then monthly assessment for 6 to 12 months in order to assess duration of resumption to normal work, improvement of symptoms, disappearance of varicocity and improvement of fertility.

RESULTS

There was wide variation of age of patients between both OV and LV groups. The ages of patients ranged between 11 years to 50 years. The mean age of LV group was 25.72±6.026 years and for OV group it was 27.58±6.694 years with p 0.325 (Table No.1).

In OV group 92.5% of patients were having left varicocele, 5% right varicocele and 2.5 bilateral disease where as in LV group 90% of cases were having left , 7.5 % right and 2.5% bilateral varicocele (Table No.1). The symptoms among patients leading to disease in both comparative groups were found almost same . These were reported as symptomless 2(5%) in O.V group and 1(2.5%) in L.V group, dragging sensation and aching pain in scrotum or groin were found in 38(95%) cases of O.V group and 39(97.5%) of L.V group, positive cough impulse was seen 15 (37.5%) of O.V group and 10 (25%) of L.V group , infertility was found in 21 (52.5%) of O.V group and 23 (57.5%) of L.V group (Table No.1) .

Data shows that there was no significant difference in grade among these groups, however majority of patients were belonging to grade III (OV=67.5% versus LV 60%) as compared to grade II(OV=32.5% versus LV =40%)(Table 1).

Table:-1: Age and site, presenting complaints and grade wise percentage of open and Laparoscopic Varicocelectomy.

Variable	Operative Procedure				
	Open Varicocelectomy		Laparoscopic Varicocelectomy		
	Number of Patients	%age	Number of Patients	% Age	
Age					
• 10-20 years	8	20%	6	15%	Mean Age : OV 25.72±6.0 years LV 27.58±6.6 years P value 0.325
• 21-30 years	22	55%	25	60%	
• 31-40 years	9	22.5%	8	20%	
• 41-50 years	1	2.5%	2	5%	
Site of Distribution					
• Right Side	2	5%	3	7.5%	
• Left Side	37	92%	36	90%	
• Bilateral	1	2.5%	1	2.5%	
Presenting Complaints					
• Symptomless	2	5%	1	2.5%	
• Dragging sensation and aching pain in scrotum or groin	38	95%	39	97.5%	
• Cough impulse	15	37.5%	10	25%	
• Infertility	21	52.5%	23	57.5%	
Grades of Varicocele					
• Grade II	13	32.5%	16	40%	
• Grade III	27	67.5%	24	60&	

Operative time ranged between 20 to 50 minutes in both groups. The mean time in OV group was 29.70±8.498 minutes and 25.08±5.558 minutes in LV group (p 0.005). The mild pain was observed in 7 (17.5%) patients of OV group and 16 (40 %) patients of LV group. Similarly, Moderate pain was observed in 23 (57.5%) patients of OV group and 20 (50%) patients of LV group. Whereas, severe pain was described by 10(25%) patients in OV group and 4 (10 %) patients in LV group (p 0.032).

The common complications seen in this study were wound infection and hydrocele. The wound infection was found in 6 (15%) patients of OV group and 2 (5%) patients of LV group . The hydrocele was seen in 5(12.5%) patients of OV group as compared 2 (5%) cases of LV group. The Residual varicocele and recurrence of varicocele was observed in two cases (2.5%) of OV group and 3 cases of LV group with value p <0.359 (Table No.2) . The duration of hospital stay varied from 1 to 5 days. It was longer about 2-3 days in 34 (85%) of OV patients as compared to LV cases where majority 36(90%) were discharged within 1 to 2 days. The mean hospital stay in OV group was 2.45±0.749 days and LV group was 1.85±0.736 days (*p* 0.001) showing significant differences in mean hospital stay in both groups (Table No.2).

Table:-2: Pain, complications and hospital stay wise percentage of open and Laparoscopic Varicocelectomy.

Variable	Operative Procedure				
	Open Varicocelectomy		Laparoscopic Varicocelectomy		
	Number of Patients	%age	Number of Patients	% Age	
Pain					
• Mild	7	17.5%	16	40%	P value 0.032
• Moderate	23	57.5%	20	50%	
• Sever	10	25%%	4	10%	
Complications					
• Wound infection	6	15%	2	5%	Over all incidence of complications; OV 32.5% LV 17.5%
• Hydrocele formation	5	12.5%	2	5%	
• Residual Varicocele	1	2.5%	2	5%	
• Recurrence	1	2.5%	1	2.5%	
Hospital Stay					
• 1 day	0	0	12	30%	P value 0.001
• 2 day	28	70%	24	60%	
• 3 day	6	15%	2	5%	
• 4 day	6	15%	2	5%	

DISCUSSION

Varicocele is a condition of varicosity and tortusity of the pampiniform plexus that is often associated with a reduction in the volume of affected testicle. Varicocele before puberty is rare and percentage of clinically evidenced varicocele in young male adults varies from 9-23% where as the disease increases to 40 percent among infertile patients[8,9] .

In this study age ranged from 11 to 50 years in both groups with high incidence in 3rd and 4th decade (OV= 77.5 % versus LV=80%).The mean age was 25.72±6.026 in OV group and 27.58±6.694 in LV group. The similar age group patients were found in other local studies as well [10] . The probable reasons include early diagnosis in those countries as a result of their regular medical checkups even at schools [11] . This study finds left varicocele as a commonest site in both groups (OV=92.5 versus LV=90%) followed by right side (OV=5% v/s LV=10 %) where as bilateral varicocele was seen in 2.5 percent cases of each group. The results coincide with the study carried out by Sangrasi AK et al in 2009. According to that Sangrasi found the patients with left unilateral varicocele in 92 % of OV group and 94 % of LV group [12] .

The dragging sensation and aching pain in scrotum or groin was the commonest presentation of patients (OV= 95% versus LV=97.5) in both group. This was followed by symptomless cases which included 5% among OV and 2.5 percent among LV group respectively. Whereas, Zucchi A [13] found 80 % patients with history of dragging sensation and aching pain. One reason towards the variations between both studies could be much early response of patients at diagnostic stages in the developed countries and poor response by the patients in developing countries including Pakistan. Varicocele was graded according to the criteria published by Lion PR et al [14]. The clinical examination revealed grade II varicocele in 32.5% of OV group and 40% of LV group and grade III varicocele in 67.5 % in OV group & 60 % of LV group . However, in study of

Sangrasi AK et al [12] 32% of the patients presented with grade II and 68% garde III and similarly Bebars GA [8] found majority of cases in garde II & III.

The operative time was longer in open varicoceletomy. The mean operative time for open varicocelectomy group was 29.70+8.498 minutes and for laparoscopic varicocelectomy was 25.08+5.558 minutes with range of 20 to 50 minutes in both groups (p value 0.005). The mean operative time of LV group reported in the present series was similar to that reported by Donovan and Winfield[15] ,Tan et al [16] and Fuse H et al [17] .In local studies the mean operative time given by Iqbal M [18] was 20 minutes for LV group and 30 minutes for OV group.

Study reveals higher postoperative pain in OV group as compared to LV group. Moderate to severe pain was observed in 82.5 % patients of OV as compared to 60% of LV group. Where as mild pain found in 17.5% of OV patients and 40% of LV cases. However other studies reveals higher postoperative pain in laproscopic group as compare to open varicocelectomy group with p values at 0.004 [12] .

Higher post operative complications were found in OV group (32.5 %) as compared to LV group (17.5) with P value of 0.359. Similar trend was recorded by Sangrasi AK [12].

This study reports hydrocele in12.5 percent of OV and 5 percent of LV group and recurrence rate at 2.5% in grade III cases of both groups. This has been well documented in different studies with higher grade of pre operative varicocele [19]. This is opposite to other studies which have reported a high rate of recurrence in laparoscopic varix ligation [20,21] .

Laparoscopic varicocelectomy has been performed by many surgeons as a day case surgical procedure [16,22,23] , the mean hospital stay after LV in this study was 1.85± 0.736 relatively shorter than OV i.e., 2.45±0.749 with p value 0.001. The findings correlate with the studies by Lynch et al [21].

The resumption to work was attributed to some cultural and social factors. Factors contributing to prolonged hospital stay are postoperative wound complication and the performance of additional operative procedure particularly inguinal hernia repair [6]. The study shows early resumption of work in LV group i.e., 2 weeks as compared to OV group i.e. 3-4 weeks days.

CONCLUSIONS

The study compares different postoperative parameters like, severity of pain, haematoma, wound infection and hydrocele in between laparoscopic and open varicocelectomy. The results shows that LV is superior than OV in terms of better cosmesis , less operative time, less complications, short hospital stay and early return to work.

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Address for Corresponding Author:
Dr. Ubedullah Shaikh
Banglow No. P-6 , New Doctor Colony
Nawabshah (SBA).
Contact No: 03332609835

Original Article

Role of Relaxant Prostaglandins in the Effect of Nebivolol on Isolated Tracheal Muscle of Guinea Pig

1. Asma Shaukat 2. Muhammad Nawaz 3. Muzammil Hasan Najmi 4. Asif Saeed

1. Asstt. Prof. of Pharmacology, AIMC, Abbotabad 2. Assoc. Prof. of Surgery, WMC, Abbotabad 3. Prof and Head of Pharmacology Department, FUMC, Rawalpindi 4. Asstt. Prof. of Surgery, WMC, Abbotabad.

ABSTRACT

Aims and Objectives: The present study was therefore aimed to evaluate the role of relaxant prostaglandins in modulating the effect of Nebivolol on tracheal muscle of guinea pig since the exact mechanism underlying its effects on tracheal muscle has not been established yet.

Background: The use of beta blockers is limited by their ability to produce bronchospasm in asthmatics. Third generation β blockers like Nebivolol may show better tolerability since there may be involvement of relaxant prostaglandins in its effect. However the involvement of prostaglandins in the respiratory effects of Nebivolol remains unexplored. The present study, carried out on isolated tracheal muscle strips of guinea pigs was designed to explore this controversy.

Study Design: Experimental Study.

Place and Duration of Study: This study was conducted at the Department of Pharmacology, Army Medical College, Rawalpindi since April 2010 to November 2010.

Materials and Methods: Varying concentration of histamine ranging from 10^{-7}M to 10^{-3}M were used to plot a concentration response curve on the isolated tracheal muscle strips of guinea pig and was used as a control. The same concentration response curve was plotted in presence of a fixed concentration of Nebivolol 10^{-6}M and then again in presence of a fixed concentration of Indomethacin 10^{-6}M and Nebivolol 10^{-6}M together in a series of experiments using six sets of isolated tracheal muscle strips in each case.

Results: Nebivolol did not produce any significant shift in the concentration response curve in the presence and absence of Indomethacin.

Conclusion: Nebivolol does not augment the histamine induced contraction of respiratory smooth muscle of guinea pig in the presence of Indomethacin, prostaglandin synthesis inhibitor indicating no role of relaxant prostaglandins in the sparing of respiratory smooth muscle by Nebivolol.

Key Words: Beta blockers, Bronchospasm, Nebivolol, Isolated tracheal smooth muscle,Histamine, Indomethacin.

INTRODUCTION

Beta adrenoceptor antagonists are one of the most effective drugs in the treatment of cardiovascular diseases as well as non cardiovascular diseases.[1]However their therapeutic utility is limited by pulmonary adverse effects.[2] This is more commonly seen with non selective β blockers. So new molecules with a better respiratory tolerability were designed to overcome the narrow therapeutic window of first generation β blockers.[3]Nebivolol is such a newer beta blocker possessing ancillary properties due to which it may afford a greater margin of safety in patients with COAD.[2]Studies have reported that Nebivolol has sparing effect on airway smooth muscle.[4,5]However the mechanism underlying this effect is still controversial, Matera, 1998[6] has implicated modulation of nitric oxide release to be responsible for this sparing effect while Tilley *et al* 2003[7] have shown relaxant prostaglandins to be responsible. Therefore the proposed study was planned to evaluate the role of relaxant prostaglandins in the respiratory effects of Nebivolol.

MATERIALS AND METHODS

Animals: The present study has been conducted on the isolated tracheal smooth muscle of 24 guinea pigs of Dunkin Hartley variety weighing 500 to 600 grams.They were housed at room temperature and were given tap water *ad libitum* and fed with a standard diet consisting of carrots, choker and grams.

Drugs used for the study: Nebivolol was a generous gift from Menarini Recerche, Italy.Histamine was purchased from Sigma Chemical Co. USA while indomethacin was bought from Shanghai Chang Hua Industry, China.

Preparation of the Solutions: Krebs Henseleit solution was used as the nutrient solution the composition of which per 1000 mls is: NaCl-118.2mM, KCl-4.7mM, $MgSO_4.7H_2O$-1.2mM, $CaCl_2$-2.5mM, KH_2PO_4-1.3mM, $NaHCO_3$-25.0mM, Dextrose-11.7mM. Solutions of all drugs were prepared in the distilled water except for Nebivolol the solution of which was prepared in Dimethyl sulphoxide since Nebivolol is highly lipophilic and insoluble in water[8].

General procedure for the experiments: The guinea pigs were killed by cervical dislocation. Chest was

opened through midline incision. The whole of trachea, from larynx to bronchi, was dissected out and was transferred to a dissecting dish containing Kreb's Henseleit solution at room temperature. The tracheal tube was cut into rings, two to three mm wide, each containing about two cartilages. Each ring was opened by a longitudinal cut on the ventral side opposite to the smooth muscle,forming a tracheal chain with smooth muscle in the centre and cartilagenous portion on the edges. The tissue preparation was then transferred to an isolated tissue bath of 50 ml capacity, containing Kreb's Henseleit solution at 37ºC and was aerated with oxygen continuously.[9] One end of the tracheal strip was attached to the oxygen tube inside the tissue bath while the other end was connected to an Isometric Force Displacement Transducer by means of a thread. The tissue was allowed a period of equilibration for 45 minutes against an imposed tension of two grams. During this period, the physiological solution in the organ bath was changed three to four times. A tension of one gram was applied to the tracheal strip continuously throughout the experiment after the initial equilibration period. The trachealis muscle activity was recorded through the transducer on Four Channel Oscillograph.

Method for the individual Experiment

Concentration response curve of histamine in normal isolated tracheal muscle of guinea pig (Group 1): After the initial equilibration period, the baseline tension was adjusted. Histamine in a concentration 10^{-3}M (18500 micrograms/100 mls) was added to the organ bath and its effect was recorded on the oscillograph, through an isometric force displacement transducer. When the effect reached a plateau, the drug was washed away from the tissue bath and the tissue was allowed to relax passively. After the baseline tension had been restored, the same procedure was repeated with other concentrations of histamine, i.e., 10^{-4}M, 10^{-5}M, 10^{-6}M and 10^{-7}M in a random order. An interval of at least ten minutes was allowed before the addition of next concentration. Six experiments were performed in the same way and the mean response for each concentration was worked out. A concentration response curve was obtained by plotting the percent contraction against the logarithm of concentrations.

Concentration response curve of histamine in the presence of fixed dose of Nebivolol (10^{-6}m) in normal (unsensitized) isolated tracheal muscle of guinea pig (Group 2): In this set of experiments, the effect of histamine on normal tracheal muscle was studied in the presence of a fixed dose of Nebivolol, i.e.,10^{-6}M.[10] After adjusting the baseline tension, Nebivolol 10^{-6}M was added to the organ bath. It was then left in contact with the tissue for 15 minutes. Then the same procedure as described for the above mentioned experiment was followed.

Concentration response curve of histamine in the presence of fixed dose of indomethacin (10^{-6}m) and Nebivolol (10^{-6}m) in normal (unsensitized) isolated tracheal muscle of guinea pig (Group 3): After adjusting the baseline tension, indomethacin at a concentration 10^{-6}M[11] was added to the organ bath to block the synthesis of endogenous prostaglandins followed by Nebivolol 10^{-6}M.The drugs were left in contact with the tissue for 15 minutes. Then histamine 10^{-3}M was poured into the organ bath in the presence of indomethacin and Nebivolol and contraction of the tissue was recorded on the oscillograph, through an isometric transducer and the same procedure as described previously was repeated. Six experiments were performed.

Statistical evaluation::The results have been expressed as Means ± Standard Error of Means. The arithmetic means and SEMs were calculated using Microsoft Office Excel 2007.In order to find the significance of the difference between two observations Student's'*t*' test was used.The difference between two observations was considered as significant if the *p* value was less than 0.05.

RESULTS

Comparison of Group 1 (Histamine alone) with Group 2 (Histamine after pretreatment with Nebivolol 10^{-6}M): In a series of six experiments, the mean $\pm$ SEM values of the responses and the percent responses to the different concentrations of histamine in the two groups are shown in the Table 1. Group 1 was taken as the control group and percent response with 10^{-3} M in group 1 was taken as 100% and responses with other concentrations were compared with it The mean values of responses produced by different concentrations of histamine when compared between Group I and Group 2 were found statistically insignificant ($P > 0.05$) (Table 1 and Figure 1). The mean percent deviations were calculated for each dose of histamine and found statistically insignificant. The mean deviation was 2.42 percent (Figure 1).

Comparison of Group 2 (Histamine on normal tissue pretreated with fixed dose of Nebivolol 10^{-6}M) with Group 3 (Histamine on normal tissue pretreated with fixed concentration of Nebivolol 10^{-6}M and Indomethacin 10^{-6}M): The mean values of responses and mean percent responses in these groups were statistically insignificant ($P > 0.05$) (Table 2 and Figure 2 & 3). The mean percent deviations calculated for each dose of histamine used in Group 2 and Group 4 were 4.04, 3.5, 1.56, 1.5 and 0.64 percent respectively. The mean deviation was 2.24 percent.

Table No.1: Comparison of responses of tracheal muscle to histamine in group 1 and 2

	Group 1	Group 2	Group 1	Group 2	Group 1	GROUP 2	GROUP 1	GROUP 2	GROUP 1	GROUP 2
Serial No.	10^{-3}M	10^{-3}M	10^{-4}M	10^{-4}M	10^{-5}M	10^{-5}M	10^{-6}M	10^{-6}M	10^{-7}M	10^{-7}M
1	79 mm	80 mm	70 mm	70 mm	50 mm	52 mm	34 mm	32 mm	14 mm	10 mm
2	75	76	63	64	51	57	32	38	12	14
3	80	84	68	76	59	62	39	40	11	15
4	79	76	60	62	50	50	28	26	10	8
5	82	80	71	69	49	50	33	31	10	13
6	81	78	68	67	49	48	30	30	12	13
Mean	79.33	79	66.66	68	51.33	53.16	32.66	32.83	11.5	12.16
SD	2.42	3.03	4.27	4.93	3.82	5.30	3.77	5.23	1.51	2.63
SEM	0.98	1.23	1.74	2.01	1.56	2.16	1.54	2.13	0.61	1.07
P VALUE	0.782^{Ns}		0.400^{Ns}		0.130^{Ns}		0.901^{Ns}		0.618^{Ns}	

p value > 0.05 = Not significant (Ns) *p* value < 0.05 = Significant (*)

Table No.2: Comparison of responses of tracheal muscle to histamine in group 2 and 4

	Group 2	Group 4	Group 2	Group 4	Group 2	Group 4	Group 2	Group 4	Group 2	Group 4
Serial no.	10^{-3}M	10^{-3}M	10^{-4}M	10^{-4}M	10^{-5}M	10^{-5}M	10^{-6}M	10^{-6}M	10^{-7}M	10^{-7}M
1	80	81	70	70	52	55	32	36	10	10
2	76	85	64	74	57	57	38	40	14	20
3	84	72	76	64	62	47	40	30	15	8
4	76	84	62	71	50	59	26	33	8	12
5	80	75	69	63	50	54	31	30	13	12
6	78	80	67	72	48	52	30	35	13	14
Mean	79	79.5	68	69	53.16	54	32.83	34	12.16	12.66
SD	3.03	5.08	4.93	4.47	5.30	4.19	5.23	3.84	2.63	4.13
SEM	1.23	2.07	2.01	1.82	2.16	1.71	2.13	1.57	1.07	1.68
P VALUE	0.88^{Ns}		0.78^{Ns}		0.81^{Ns}		0.65^{Ns}		0.79^{Ns}	

p value > 0.05 = Not significant (Ns), *p* value < 0.05 = Significant (*)

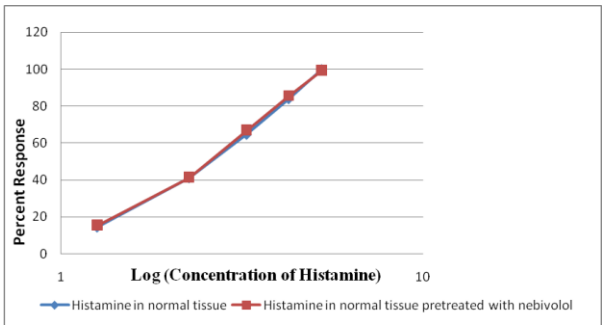

Figure No. 1: Log concentration-response curves of histamine in guinea pig tracheal smooth muscle in the absence (Group 1) and presence of fixed dose (10^{-6}M) of Nebivolol (Group 2).

DISCUSSION

In the first set of experiments, effects of different concentrations of histamine were studied on normal isolated tracheal muscle of guinea pig. When isolated tracheal muscle was pretreated with a fixed concentration of Nebivolol (10^{-6}M) it did not produce statistically significant effect. From these findings, it is inferred that Nebivolol has a sparing effect on histamine-induced contractions of tracheal smooth muscle. These findings support the results of *in vivo* study by Agostino *et al.*, (2001)[5] whereby Nebivolol did not affect airway responsiveness to inhaled histamine in rabbits. Similar findings have been reported in other *in vivo* studies.[12]

Some aspects concerned with the mechanisms that may be responsible for the lack of bronchoconstrictor effect of Nebivolol on tracheal muscle were also explored. There may be many possible mechanisms which can explain its sparing effect. First mechanism is related to its β_1 selectivity. It is the most selective β_1-adrenoceptor antagonist currently available for clinical

use.[13,14,15]Beta 1 receptor selectivity is an important determinant of less incidence of bronchoconstriction seen with cardioselective blockers such as Metoprolol and Atenolol as compared to non selective antagonists[16].De Clerck *et al*., (1989)[4] compared the bronchoconstrictor effects of atenolol, Nebivolol and propranolol in guinea pigs and they reported that bronchoconstriction was greatest with Propranolol followed by atenolol while Nebivolol had sparing effect. Van Zyl *et al*., (1989)[17]and Fogari *et al*. (1990)[16]

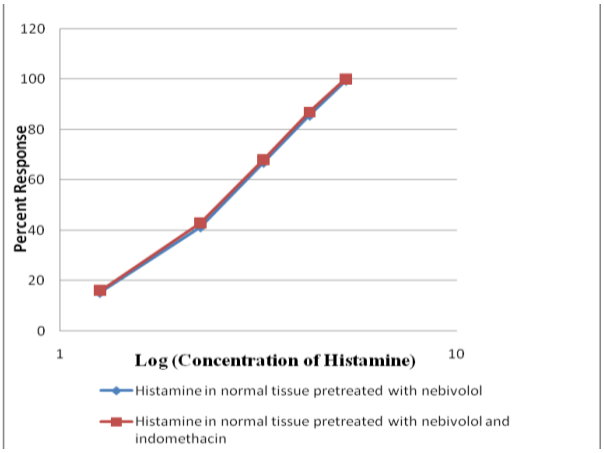

Figure 2: Log concentration-response curves of histamine in normal (unsensitized) isolated guinea pig tracheal muscle in Group 2 and Group 3.

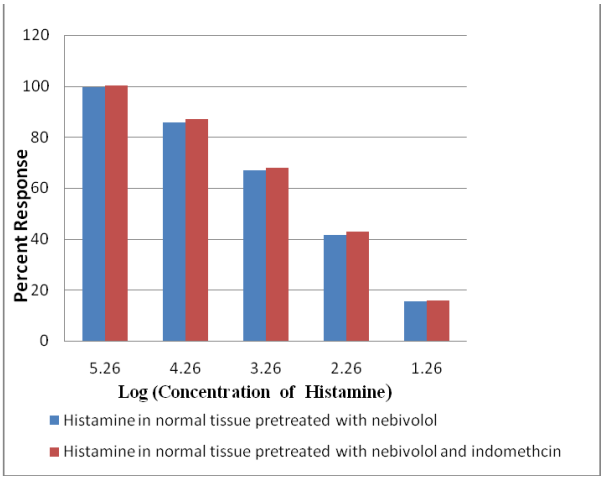

Figure 3: Bar diagram showing histamine induced contractions in normal isolated guinea pig tracheal smooth muscle in Group 2 and Group3.

carried out studies in asthmatic patients and had same results. So the different effect of Nebivolol can not be fully explained by its β_1 selectivity.Also Nebivolol lacks partial agonist activity at β_2 receptors.[18,19] So this mechanism is not plausible.

Other mechanisms apart from β_1 receptor selectivity i.e. relaxant prostaglandins may be involved in its sparing effect.Their involvement was therefore evaluated and a set of experiments was designed. The tracheal muscle was pretreated with indomethacin in a concentration of 10^{-6}M and Nebivolol 10^{-6}M. The concentration response curve was then constructed using different concentrations of histamine.This concentration response curve and its parameters were compared with the curve obtained with histamine in tracheal muscle pretreated with Nebivolol 10^{-6}M alone. Though mean $\pm$ SEM of maximum contraction increased from 79 $\pm$ 1.23mm to 79.5 $\pm$ 2.07mm, the difference was statistically insignificant.Similarly percent responses for other concentrations and percent deviation was statistically insignificant.

Prostaglandins of the E series have been shown to mediate inhibition of the respiratory smooth muscle in rabbit, guinea pig, sheep and pig and it has been suggested that PGEs play an important role in maintaining bronchial tone in asthmatic patients.[7] It has also been demonstrated that drugs which inhibit the cyclooxygenase pathway of arachidonic acid metabolism can reduce the effect of a relaxant prostaglandin such as PGE_2.[20] Had there been involvement of relaxant prostaglandins in the effect of Nebivolol the effect should have been blocked by inhibition of synthesis of prostaglandins by indomethacin and curve would have shifted upwards and to the left, but there was no significant change in this study, so the above mentioned possibility of involvement of relaxant prostaglandins could not be substantiated experimentally.

CONCLUSION

The involvement of relaxant prostaglandins in the sparing effect of Nebivolol could not be substantiated experimentally indicating the involvement of some other mechanism.

RECOMMENDATIONS: Further exploratory work is recommended to elucidate the exact mechanism underlying the sparing effect of Nebivolol against histamine-induced contraction of isolated guinea pig trachea.

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Address for Corresponding Author:
Asma Shaukat,
Assistant Professor,
Pharmacology Department,
Abbottabad International Medical College,
Abbottabad
E.mail: a_shaukat11@yahoo.com
Tel. No.+92-992-331588.

Original Article

The Comparative Role of Optical Urethrotomy with and without Clean Intermittent Self Catheterization (CISC) in Urethral Stricture

1. Muhammad Ali Suhail 2. Shafique-ur-Rahaman Memon 3. Ubedullah Shaikh

1. Asstt. Prof. of Urology, PUM&HSW, Nawabshah, Sindh 2. Prof. of Urology, LUM&HS, Jamshoro Sindh
3. PG Student, M.S. General Surgery, LUM&HS, Jamshoro Sindh

ABSTRACT

Objective: To assess the comparative role of optical urethrotomy in urethral strictures with (CISC) clean intermittent self catheterization and with out CISC.

Study Design: comparative cross sectional.

Place and Duration of Study: This study was conducted at the Department of Urology Peoples University of Medical and Health Sciences for Women. Nawabshah. Sind from July 2008 to June 2010.

Materials and Methods: The patients were thoroughly evaluated. All patients were subjectively examined pre-operatively by detailed history and complete clinical examination. Patient's satisfaction from his urinary stream and the sense of satisfactorily emptying of bladder were the main subjective tool. While the Uro-Flow Metry and Post-voiding residual urine were the main objective tools in both pre and post operative period. Under the spinal anesthesia optical internal urethrotomy was done. After removal of catheter all patients were divided equally in two groups.

Group A. Patients without clean intermittent self Catheterization (CISC).

Group B. Patients on clean intermittent self catheterization (CISC).

Results: All hundred (100) subjects were divided in two groups. Group A &B.Fifty (50) in each group. After third month seven (07) patients of group A, showed decline uro-flow Metry. Two (02) subjects in fifth month were submitted for the second session of optical urethrotomy. In Seventh month three (03) patients presented acute retention of urine all three were submitted for second session of optical urethrotomy. In 12th month five patients more submitted for the repeat session of optical urethrotomy regarding the group B patients. In the seventh month (05) patients presented with disturbed flow metry. In tenth month two (02) while in twelth month three (03) patients were needed to the second and third sessions of urethrotomy respectively.

Conclusion: we conclude that optical urethrotomy with CISC is more effective treatment modality for the urethral strictures than the optical urethrotomy without CISC.

Key Words- Optical urethrotomy , urethral stricture, comparative treatment, clean intermittent self catheterization.

INTRODUCTION

Until 30 years ago stricture of urethra were managed by the traditional periodic dilatation, supplemented from time to time by blind internal urethrotomy with Otis instrument to keep the channel open. Reconstructive urethral surgery though carries higher success rate but needs expertise and is not the first line treatment of every stricture.[1] The urethral stricture begins as a fibrosing lesions of urethral mucosa with lumen reduction and resultant in symptom complex. A 50% reduction of urethral circumference reduces the lumen size about 25% and produces significant urodynamic disturbance. [2] Urethral stricture diseases remains the complicated problem for the mankind since thousands of years. No one technique is suitable for all types of the stricture and the surgeon should be familiar with the different techniques and choose the most suitable one according to the case he deals with.[3] Urethral strictures are a frequent source of lower urinary tract disorders in adults, such as urinary tract infection, acute urinary retention, high-pressure voiding leading to secondary bladder thickening and irritability and even bladder diverticulae or perineal fistulae and abscess [4]. Blunt perineal trauma, urethral catheterization or instrumentation and sexually transmitted diseases are the most frequent causes of strictures. However, most causes of urethral strictures remain unknown, but they are probably the result of a remote unrecognized perineal trauma experienced during childhood.[5] Surgical treatments of urethral stricture diseases is a continually evolving process, and currently there is renewed controversy over the best means of reconstructing the urethra. Moreover, the superiority of one technique over another has not yet been clearly defined. Urologists must be familiar with the use of numerous and various surgical techniques to deal with any condition of the urethra during surgery. [6] The aim of treatment is to restore the urethral continuity. The periodic dilatation has been reported the oldest mean of treatment. Later on it was supplemented by blind internal urethrotomy.[7] In the last thirty years, clean intermittent catheterization of urinary bladder has proven to be one of the most important advances in

Urology. The cost effectiveness of different catheters and the lack of education limit the use the of this procedure.[8] Throughout medical history, the treatment of urethral strictures ranged from catheterization, the insertion of bogies to different methods of dilation, blind internal urethrotomy, and open surgery. The rise of endoscopy in the 19th century added the possibility of direct vision internal urethrotomy to this therapeutic spectrum. The development of this endourologic method is recapitulated from the first report in 1865 to the gold standard of cold knife urethrotomy in 1971 and later modifications e.g. advanced laser techniques.[9] The results of internal urethrotomy were more favorable when the operation was performed in a solitary, short (less than 2 cm) non-infected stricture of the proximal urethra. The poor results (38%) were reported in cases of extensive strictures situated in the distal urethra or in patients with a history of urethral surgery. [10] Endoscopic treatment should be considered the first line procedure for all post-traumatic posterior urethral strictures. The morbidity of open surgery can be avoided in 61% of patients. Hospital stay, loss of work, morbidity and related complications are also markedly decreased with Endoscopic therapy. [11] Martov AG assessed the efficacy of internal urethrotomy made in total of 802 patients aged from 16 to 89 years (mean age 58.6 years) with urethral stricture in 1994-2004. Internal optic urethrotomy was made in 733 cases with a cold knife, in 52--with electric knife and in 17 cases--with laser. He concluded that internal optic urethrotomy is an effective therapeutic method. After primary urethrotomy recurrences of the strictures to be re-operated reach 19.6%. These can be successfully managed by endoscopic re-operations and rehabilitation measures like CISC (clean intermittent self catheterization.) [12] The direct vision cold knife internal urethrotormy (DVU) was found simple, quick and cost effective mode of operation in urethral strictures in maintaining acceptable voiding patterns. Direct vision cold knife internal urethrotomy is a simple, cost effective and versatile method of treatment in urethral strictures which is attractive where resources are scarce. [13]

MATERIALS AND METHODS

The patients were collected from the Department of Urology Dialysis and Lithotripsy centre at Peoples Women medical University for girls Nawab shah. Shaheed Benazir Abad Sind.

The patients were thoroughly evaluated subjectively and objectively in pre and post operative period. All patients were subjectively examined pre-operatively by detailed history and complete clinical examination. Patient's satisfaction from his stream and the sense of satisfactorily emptying of bladder were the main subjective tool in pre and postoperative period. While the Uro-Flow Metry i.e. of urinary flow rate per second and ultrasound scan for the measurement of Post-voiding residual urine were the main objective tools in both pre and post operative period. For the assessment of renal function, serum creatinine was done in all those cases who presented with chronic retention of urine. To decide the length and site of stricture preoperatively ante-grade and retrograde urethrogram were done. Before surgery all patients were submitted for the anesthetic assessment. Under the spinal anesthesia optical internal urethrotomy was done with cold knife. After surgery 16 Fr Foley catheter was placed in all cases through half moon sheath. The remained catheterized for two to three weeks. After removal of catheter all patients were divided equally in two groups.

Group A: Patients without clean intermittent self Catheterization (CISC).

Group B: Patients on clean intermittent self catheterization (CISC).

A regular follow up was established for both groups. A first follow-up visit was after 15 days. Later on follow up was done on monthly basis. The following subjective and objective assessment was done in each follow-up visit. Patient's satisfaction from his stream and the sense of satisfactorily emptying of bladder, (UFM) Uro-Flow Metry and PVR. Post-voiding residual urine. After the catheter removal a base line level of both these variables .I.e. Uro-Flow Metry (>12mls/sec) and Post-voiding residual urine (<50c.c) was set and further results in each follow-up were compared with it. Female sex and pediatric age below 14 years were excluded from this study.

RESULTS

All hundred (100) subjects, fifty (50) in each group i.e. group A & B were objectively assed in each follow-up. The results up to third month of the optical urethrotomy were remained almost same as those of the base line level i.e. (Uro-Flow Metery >12mls/sec) and (Post-voiding residual urine <50c.c) in both groups. After third month seven (07) patients of group A, showed decline uro-flow Metry i.e. from base line of >12mls/sec to average flow of 10mls /sec but with maintained post voided residual volume of base line level. Though the total time in uro-flow Metry in these subjects were increased but these seven subjects successfully emptied their bladder. While the fifty (50) subjects of group B, weekly performing the Clean Intermittent Self Catheterization (CISC), maintained their base line level without any change in uro-flow metry and post voided residual volume. In fifth month, among group A, twelve (12) patients presented with the sign of bladder out let obstruction. Two (02) subjects out of these twelve were in acute retention of urine. Due to failed urethral catheterization Supra-pubic catheterization was done in both cases of urinary retention. Later on these two subjects were submitted

for the second session of optical urethrotomy. While remaining ten (10) patients presented with decline in urinary flow rate, than the baseline level i.e. <10mls/sec and increased post voided residual volume i.e. more than 60c.c. In seventh month of postoperative period three (05) patients presented with complain of retarded stream and straining in micturation. Out of these five patients three (03) subjects went in to acute retention of urine which was dealt by supra pubic catheterization. Later on these three subjects were also submitted for second session of optical urethrotomy. Eight (08) more patients, among the group A, in the 9th month of first session of optical urethrotomy, presented with the decreased urinary flow rate and increased post voided residual volume. In the last month of follow-up period i.e. the 12th month of optical urethrotomy three (03) patients along with two (02) subjects, having second session of optical in the 5th month, total five (05) more patients of group A presented with the signs of bladder out let obstruction. In All of these five subjects urinary flow rate was below 6mls/sec and post-voided residual urine was >100c.c. on the basis of these findings all five subjects were submitted for the second session in three patients while third session of optical urethrotomy in two subjects was given. only twenty (22) out of fifty (50) subjects of group A maintained the base line level of their urinary flow rate and post voided residual volume i.e.>12mls/sec and <50c.c respectively up to the last follow-up month. All the fifty (50) subjects belonging to the group B maintained their base line level of urinary flow rate and the status of post-voided residual urine up to the sixth post operative month. In the 7th post-operative month five (05) patients presented with decreased flow rate than the base line level i.e between 10 to 12mls/sec but the post voided residual fraction of urine in all these five cases remained below 50.c.c. which was the initial base line level. Another two (02) patients in group B presented in acute retention of in 10th month of follow-up. Both were submitted for the second session of optical urethrotomy. Six (06) patients of this same group presented with the signs of bladder out let obstruction in the last month of follow –up i.e. 12th month. In three (03) patients out of these six subjects urinary flow rate was less than 10 mls/sec while post-voided residual urine was more than 100c.c. These three (03) subjects were submitted for the second session optical urethrotomy followed by Bi-weekly CISC. Other three (03) subjects among these six patients were maintaining their residual urine below 100 c.c and their flow rate was around 10 mls/sec. Out of 50 patients of group B total thirteen (13) subjects' (26%) presented with signs of bladder out let obstruction after having first session of optical urethrotomy followed by CISC. Out of these thirteen patients five (05) subjects received third session of optical urethrotomy to maintain their base line level of both variables i.e. residual urine and uro flow metry.

Table No.1: A Base Line Level of Objective Variables

Variable	**Base line level**
URO-Flow Metry	Average urinary flow rate of > 12mls/sec.
Abdominal Ultra Sound	Post-voided residual urine <50 c.c

Table No.2: Groups

Group	Description	No. of Patients	Total
A	Optical urethrotomy without CISC.	50	
B	Optical urethrotomy with CISC.	50	100

Table No.3: Groups (A)

Follow-up month	Response to optical urethrotomy.	No: of Session	total Patients
3rd month.	Base line remained maintained.	1st	All 50 pts.
4th month	Decreased AVF— 10mls/sec But maintained PVR.	1st	07
5th month	02 subjects AROU 03 AVF 10mls/sec & PVR 60-100	2nd	05
7th month	03 subjects AROU.	2nd	03
9th month	Decreased AVF<10mls/sec PVR around 100 c.c	1st	08
12th month	03 patients of 7th month 02 patients. AVF <6mls/sec.PVR > 100 c.c	3rd 2nd	05

DISCUSSION

A thorough understanding of urethral anatomy and etiology of urethral stricture followed by an effective treatment are very crucial if successful outcome is required.[14] Clean intermittent self-catheterization is often proposed to patients with bladder emptying disorders. [15] In our comparative series all 50 patients of group A were submitted for the optical urethrotomy without CISC. Only 22 (44%) out of 50 could maintain their base line level of residual volume and uro-flow metry up to the end of first year with out any sign of bladder out let obstruction or any further session of

urethrotomy. Among the remaining 28 subjects (46%) of group A, 07 patients needed two session of optical urethrotomy while 03 patients needed third session of optical in order to maintain the base line level of the of both variables up to the end of 12th month.

Table No.4: Groups (B)

Follow-up month	Response to optical urethrotomy.	No: of session	Total patients
Up to 6th month.	Maintained their base line level of both variables..i.e. AVF &PVR	1st with CISC	50
7th month.	AVF 10-12mls/sec but Maintained PVR of base line.	1st with CISC	05
10th month.	02 Patients in AROU (Acute retention of urine)	2nd with CISC.	02
12th month.	03 patients AVF <10 & PVR > 100 03 pateints AVF 10 & PVR < 100.	2nd with CISC CISC	06

Table No.5: Sessions of Optical Urethrotomy in Group A & B

Group	No: of session.	No: of patients.	Total.
A	1st 2nd 3rd	40 07 03	50
B	1st 2nd	45 05	50

The 50 patient of group B after first session of optical urethrotomy were put on regular Bi-weekly CISC. With this set up only 13 (26%) out 50 subjects presented with the signs of failure of optical urethrotomy. Out of these 13 only five (05) patients needed second session of optical urethrotomy. This reflects that the efficacy of optical urethrotomy with CISC is more superior than without CISC in terms of maintaining the base line of both variables and decreases the recurrence rate of stricture urethra. We in our series put the patients of group B on CISC for twice in week. Greenwell TJ et al, out of 126 patients with urethral strictures having optical urethrotomy put 50 patients Bi-weekly on CISC.[16] The concomitant use of self catheterization increases the cost effectiveness of this procedure.[17] van et al in his series has emphasized that education of the patient for the adherence to clean intermittent self catheterization and he recommends the favorable out come of CISC in bladder out let problems.[18] Rijal A in his study of 310 urethral strictures patients concluded that optical urethrotomy with CISC is more effective in preventing the recurrence of urethral strictures as compared to the Endoscopic procedure done alone.[19] Duloca V describe the importance of the selection of the surgical procedure for the urethral stricture in order to have successful out come especially he describe the place of urethraplasty.[20]

CONCLUSION

From our study of 100 patients we conclude that the optical urethrotomy with clean intermittent self catheterization (CISC) is comparatively more effective treatment of urethral strictures than with out CISC. It lowers the recurrence rate of urethral stricture which is higher after the optical urethrotomy without CISC.

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Address for Corresponding Author:
Dr. Muhammad Ali Suhail,
Assistant professor of Urology,
Peoples University for Medical & Health Sciences for Women, Nawabshah. Sindh.

Original Article

Evaluation of Centella Asiatica for its Neuropharmacology

1. Rafi Akhtar Sultan 2. Rahila Najam 3. Iqbal Azhar 4. Bushra Riaz 5. Abeer Adil 6. Zafar Alam Mahmood

1. Ph.D. Student, of Pharmacognosy 2. Assoc. Prof. of Pharmacology 3. Assoc. Prof. of Pharmacognosy 4. M.S. Student of Pharmacology 5. M.S. Student of Pharmacology, Faculty of Pharmacy, University of Karachi 6. Country Manager Pakistan, Gulf and Middle East Region, Colorcon Limited, UK.

ABSTRACT

Objective: To determine the effect of Centella Asiatica on Neuro pharmacological activities as memory, behavior (anxiety, depression).

Study Design: Experimental Study.

Place of study: This study was conducted in the department of Pharmacology, Faculty of Pharmacy, University of Karachi, Karachi from 15th March 2011 to 30th April, 2011.

Materials and Methods: Albino mice and albino rats were used. Animals were divided into control and treated groups (10 animals each). Neuro pharmacological parameters were assessed using standard techniques as Stationary rod activity, Swimming induced depression (FST), Open field, Light and dark box test and water maze model. Control group was maintained on distilled water and treated group was fed with 8.3 mg/kg Centella asiatica for 10 days. Observations were taken on 1st, 5th and 10th days.

Results: The results showed decline in the elapsed time taken by animal to reach the platform in Stationary rod and water maze model, significantly enhanced struggling time in FST, decreased number of peripheral square crosses but relatively increased central square crosses on 10th day in open field test and increased time spent in light box in Light and dark box model.

Conclusion: It can be concluded that Centella asiatica enhances memory and show antidepressant activity on acute administration while chronic use results in anxiolytic behavior.

Key Words: Centella asiatica, Cognition, Anxiolytic, Parkinsonism, Alzheimer's disease.

INTRODUCTION

Pakistan is renowned for treating different illnesses with medicinal plants especially the Unani system of medicine which has been established since Indus valley civilization [1]. One of the medicinal plant Centella asiatica belongs to the family Umbelliferae (synonymous known as Apiaceae) is distributed widely in South America and Asia especially in the damp and marshy places throughout India. The plant is richly employed in the Ayurvedic and unani systems of medicine in different forms either as whole plant, fresh leaves or in extract form [2]. The local names of plant are Vallarai in Tamil, Mandukaparni in Sanskrit, Indian Pennywort in English [3] and the Barhami boti in Urdu[4]. Centella asiatica is reported to be used as a brain tonic for enhancing memory. One such formulation of this plant is Gotu kola which is claimed to alleviate anxiety, insomnia and improve overall brain function. Centella asiatica is also the ingredient of herbal medicine mixture Medhya Rasayana. Centella asiatica is effective in improving general mental ability and cognition in mentally retarded children and in people with cognitive dysfunction[5,6,7,8]. Centella asiatica also possess antioxidant properties, capable of protecting brain against age related oxidative damage[9]. Studies also revealed that the administration of Centella asiatica is associated with the protection of brain against neurodegenerative disorders as Parkinsonism and Alzheimer's disease[10,11]. In Alzheimer's disease animal model the use of Centella asiatica extract showed decline in amyloid beta levels in hippocampus region of brain[11]. The fresh leaf extract of this plant proved efficacious in improving learning and memory[12,5,6,7]. In the study including neonatal rats (during growth spurt period), the use of fresh leaf juice of Centella asiatica resulted in increased memory [13] but according to another research Centella asiatica is involved in the retention of a learnt task for a longer period but did not accelerated the learning process as expected[14]. Different clinical studies revealed that Centella asiatica increases the level of neurotransmitters involved in learning and memory like Ach, noradrenaline, 5HT, dopamine, GABA[15,16,17,18].

MATERIALS AND METHODS

Ethanolic extract of plant: The plant material was collected from Tehsil Kahuta district Rawalpindi, Pakistan and identified by qualified taxonomist, the plant material was dried under shade and soaked in ethanol for two weeks at room temperature. After two weeks the ethanolic extract was filtered and dried by using rotary evaporator.

Animals: Albino mice (avg wt = 24 g) and albino rats (avg wt =250g) were used for the experiments and they

were fed with commercial diets. Following preliminary experiments, an optimum dose of 0.2mg was arrived for mice and 2mg for rats. The standard dose was 8.3mg/kg[19]. Extract was administered orally for 10 days.

Effects of centella asiatica on neuropharmacological activities in mice and rats: The effects of Centella asiatica on a number of neuropharmacological activities were assessed using standard techniques as described below:

Stationary rod activity: Mice were given a short training period (2 or 3 trials), before treatment. This pre-treatment training ensures mice ability to walk across a horizontal steel rod (5/8″ in diameter and approx 2 ft long) positioned 18″ at a height above the surface of the table. Mice were placed on the mid-point of the rod individually and were forced to walk towards a platform at either end of the rod[20].

Swimming induced depression: The test method used for assessing antidepressant activity was discovered by Porsolt and coworkers in 1977. The FST apparatus consists of clear water bath (20cm height × 12cm diameter) and filled with 15cm deep water. The mice were allowed to swim in a FST apparatus for 10min after that period they were returned to their home cages. On fourth day chronic mild stress 1 (CMS-1) was applied to mice i.e. tilting of cage more than 30 degree from horizontal for 48 hours. On seventh day animal were exposed to CMS-2 i.e. 200ml of water was poured on the sawdust bedding of mice home cage for 24hours [21] and on ninth day CMS-3 was applied i.e. deprivation of animals from food for 24 hours [22]. At the end of 10th day animals were allowed to swim again for 5 min and struggling time was noted. The same procedure was adopted for control and treated mice.

Open field: Open Field Method was essentially as described by Haleem and coworkers [23]. The activities were scored by counting the number of squares crossed by individual mouse during a 10 minute period [24].

Light and dark test: The apparatus comprises of a box with two compartments (20 × 20 cm). One compartment is illuminated with light and the other is kept dark. Individual animal is placed in the center of the illuminated compartments; facing one of the dark places as well the number of entries in each space and time spent in light and dark compartment is recorded for 10 minutes respectively [25].

Water maze test for rats: Water maze was developed by Richard Morris at the University of St Andrews in Scotland [26, 27]. In this test rats were placed in a pool of water facing the pool-side to avoid bias and required to escape from water onto a hidden platform whose location can normally be identified only using spatial memory. The time taken by rats to reach the platform was noted [28].

RESULT

The effect of oral administration of Centella asiatica for 10days on different CNS parameters is shown in the following tables.

Table No 1: Effect of drug on stationary rod activity.

Time in seconds required to reach the platform						
Groups	Day 1	t-test	Day 5	t-test	Day 10	t-test
Control	107 ± 0.82	**p< 0.001	6.30 ±2.63	IS	3 ± 1.63	IS
Treated	97 ± 0.876		4 ± 1.63		2 ± 0.816	

Values are mean ± SD
n=10 = total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

Table No 2: Effect of drug on open field activity.

Table No 2.1: Effect of Drug on Central Square Crossing:

Number of central square crosses						
Groups	Day 1	t-test	Day 5	t-test	Day 10	t-test
Control	28.7± 5.48	**p< 0.001	22.2± 5.81	**p< 0.001	13.2± 2.66	IS
Treated	9.4± 4.78		4.2± 1.75		12.4± 7.63	

Values are mean ± SD
n= 10= total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

Table No 2.2: Effect of Drug on Peripheral Square Crossing.

Number of peripheral square crosses						
Groups	Day 1	t-test	Day 5	t-test	Day 10	t-test
Control	103.7 ±35.4	IS	134.4 ±17.9	**p< 0.001	83.8± 14.7	**p< 0.001
Treated	94.1± 9.28		38.8± 16		12.4± 7.63	

Values are mean ± SD
n= 10= total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

Table No 3: Effect of drug on light and dark box activity.

Time in seconds spent in illuminated box						
Groups	Day 1	t-test	Day 5	t-test	Day 10	t-test
Control	78.2± 43.2	IS	60.6± 57.1	IS	10.6± 4.84	**p< 0.001
Treated	41.7± 13.2		43.3± 20.9		33.7 ±12	

Values are mean ± SD
n= 10= total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

Table No 4: Effect of drug on water maze activity.

Time in seconds to reach the platform						
Groups	Day 1	t-test	Day 5	t-test	Day 10	t-test
Control	22±0. 816	**p< 0.001	2.2± 0.789	IS	1.5± 0.471	IS
Treated	18±1. 63		1.2± 0.789		2± 0.816	

Values are mean ± SD
n= 10= total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

Table No 5: Effect of drug on FST activity.

Struggling time in sec						
Groups	Day 1	t-test	Day 10	t-test	Day 13	t-test
Control	227.9 ±34.9	IS	211.5 ±22.8	IS	258± 6.04	**p< 0.001
Treated	234.5 ±11.1		211± 38		290± 8.54	

Values are mean ± SD
n= 10= total number of animals
*p<0.01= Significant difference by t-test
**p<.001= highly significant difference from the control following t-test
IS= insignificant difference by t-test

DISCUSSION

In the present study the plant Centella asiatica was evaluated for its neuro pharmacological effects. It was observed that after the administration of Centella asiatica, the animal crossed the stationary rod in lesser time as compare to control. This effect suggests that Centella asiatica enhances learning and memory. The possibility of this outcome may be because of the fact that Centella asiatica stimulates cholinergic system [29]. The effect of this drug on water maze activity also support the above finding, as the time taken by treated animal to reach the platform was decreased considerably as compare to control. Previous clinical studies on Centella asiatica extract also revealed the presence of memory enhancing effect of this plant [12,5,6,7].

The open field activity especially the peripheral square crosses was decreased significantly literature survey denote that Centella asiatica does not induce locomotor activity, thus does not improve open field exploratory behavior [29]. This finding may be based on the fact that Centella asiatica possess anxiolytic profile which made the animal comfortable enough to decrease open field exploration. In open field model, the central square crossing is the most coherent behavior which demonstrates anxiolytic activity [30] and our study shows that on acute dosing the number of central square crosses are decreased but relatively increase on day 10, comparable to control, give rise to the premise that Centella asiatica shows anxiolytic effect on chronic administration.

Light and dark box test is based on instinctive characteristic of rodents to dislike brightly illuminated areas and on the extemporaneous exploratory behavior of rodents in response to mild stressors, i.e. novel environment and light [31]. According to our study the time spent in light box is decreased on day 1 and day 5 but increased on day 10. This result also witness the anxiolytic effect of plant on chronic use.

Forced swimming test is the behavioral paradigm used to measure the effect of antidepressant drugs [32]. In our research the struggling time was increased significantly which revealed that the plant has antidepressant property. After the acute administration of Centella asiatica showed prolonged struggling time as compare to control leading to the assumption that the plant might possess antidepressant profile on acute administration.

CONCLUSION

On the basis of above finding it can be concluded that Centella asiatica enhances memory, decreases exploratory behavior and show antidepressant activity on acute administration while anxiolytic behavior on chronic use.

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Original Article

Laparoscopic Cholecystectomy: An Experience of 550 cases at Sukkur

1. Khush Muhammad Sohu 2. Shahid Hussain Mirani 3. Ghulam Haider Rind
4. Syed Qarib Abbas 5. Azhar Ali Shah 6. Faiza Abro
1.Asstt. Prof. 2. Assist. Prof. 3.Assoc. Prof. 4.Prof. 5. Assist. Prof. 6.House Surgeon, Dept. of Surgery, Ghulam Mohammad Mahar Medical College Sukkur / Shaheed Muhtarama Benazir Bhutto Medical University Larkana

ABSTRACT

Objective: To see the results and complication rate of Laparoscopic cholecystectomy at Sukkur
Study Design: Prospective Study.
Place and Duration of Study: This study was conducted at Ghulam Mohammad Mahar Medical College Hospital Sukkur and Sukkur Blood Bank Hospital from December 2004 to December 2009.
Materials and Methods: the study comprises of 550 case. All were admitted from OPD of both hospitals. All patients had routine investigations, Liver function tests and ultrasound abdomen. The patients who underwent laparoscopic cholecystectomy whether successful or converted were included in study. The procedure was carried out by standard four port technique. Clinical examination, investigations, operative time, postoperative complications, reasons for conversion and hospital stay were recorded on proforma and results were drawn.
Results; The male patients were100 and female patient were 450, male to female ratio was 1:4.5. Mean age of patients were 47.63 years ranging from 25years to 75years there were 127 (23.09%) obese, 72 (13.90) controlled hypertensive. Anatomical obstacle noted in 40 (7.27%) patients. Adhesions in 52 (9.45%) and acute cholecystitis in 22 (3.75%) patients. Overall conversion rate was 4%. In total of 22 patients which were converted, causes were slipped clip 2, hemorrhage from falciform ligament 1, severe hemorrhage 3, unclear anatomy 6, common bile duct injury 4, intra abdominal adhesions 4, gangrene gall bladder 1, and advance carcinoma 1. Mean hospital stay was 1.8, ranges from 1 day to 10 days.
Conclusion; Laparoscopic cholecystectomy has a gold standard procedure. It is safe and effective and becoming cost effective day by day. Incidence of complication is low, morbidity and mortality are low. The pain free postoperative period and early ambulation lead to saving of value able working hours.
Key Words: Gall stones, laparoscopic cholecystectomy

INTRODUCTION

The introduction of laparoscopic cholecystectomy is an important milestone in surgical practice and superior to open cholecystectomy and heralds the development of further minimally invasive techniques. Since it's debut by Robert mourret in 1987, laparoscopic cholecystectomy has emerged as gold standard as regards laparoscopic surgery. The advantage of laparoscopic approach is the deduction of trauma of access, without compromise to exposure of operative field. This enables accelerated patient recovery and reduction of wound related complications. In Pakistan cholecystectomy is the most common elective abdominal operation with over 50,000 operations performed annually[1,2]. It was only after the event of laparoscopic cholecystectomy performed by Mouret et al 1987 in France, that general surgeon suddenly became interested in application of laparoscopy[1-4].

On one hand it offers remarkable advantage of minimal trauma in surgical access to gall Bladder, much better pain relief after surgery, leading to early ambulation and on other hand consequent reduction in operative and reparatory complication, and thus early return to work. Recently some refined studies have indicate that the metabolic response to operative trauma immunosuppression is much less in Laparoscopic cholecystectomy with advantage for both patient and surgeons[5, 6]. Ability to provide high quality and cost effective care has made ambulatory surgery one of the fastest growing era in the health care system all over the world [7].

Through initially, there was some relative contraindication, but with experience and improvement of equipment, there is contraindication. How ever in obese, abscure anatomy, adhension, hemorrhage damage to common bile duct and in acute cases, surgeon should be careful and willing to convert if necessary[6-8]. In our study, main focuses was a complication of laparoscopic surgery and its comparison with literature and thus highlight the safety and effectiveness of procedure.

MATERIALS AND METHODS

Over a period of 5 years from December 2004 to Dcember 2009, 550 laparoscopic cholecystectomies were carried out at Ghulam Muhammad Mahar Medical College Hospital Sukkur & Sukkur Blood Bank Hospital Sukkur. All patients had routine investigations, liver function tests and ultrasound of abdomen.

The patients which were selected for laparoscopic cholecystectomy, were included in the study. Those patients which were unfit due to aesthesia or any other problem and did not opted for laparoscopic cholecystectomy, were excluded from the study. The procedure was carried out by standard four port technique.

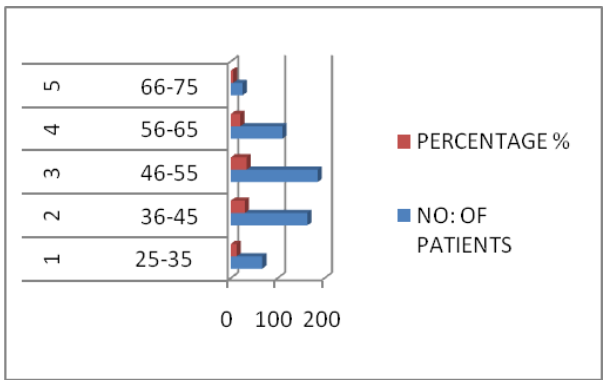
Clinical examination investigations, operative time, postoperative complication, reasons for conversion if converted and hospital stay were recorded on proforma and result were drawn.

RESULTS

The male patients were 100 and female patient were 450, male to female ratio was 1:4.5. Mean age of patients were 47.63 years ranging from 25years to 75years (Table No.1) there were 127 (23.09%) obese, 72 (13.90) controlled hypertensive. Anatomical obstacle noted in 40 (7.27%) patients. Adhesions in 52 (9.45%) and acute cholecystitis in 22 (3.75%) patients.

Table No.1: Age distribution in 550 cases

Sr. No.	Age of patients	No: of Patients	Percentage %
1	25-35	67	12.18
2	36-45	163	29.72
3	46-55	185	33.56
4	56-65	110	20
5	66-75	25	4.54



Tables No.2: Reasons of Conversion in 550 cases

Sr. No:	Causes	No: of Cases	Percentage %
1	Severe hemorrhage	6	1.10
2	Unclear Anatomy	6	1.10
3	CBD injury	4	0.73
4	Intra abdominal adhesions	4	0.73
5	Gangrenous gallbladder	1	0.17
6	Advance carcinoma	1	0.17

Overall conversion rate was 4%. In total of 22 patients which were converted, causes were slipped clip 2, hemorrhage from falciform ligament 1, severe hemorrhage 3, unclear anatomy 6, common bile duct injury 4, intra abdominal adhesions 4, gangrene gall bladder 1, and advance carcinoma 1 (Table No.2). Mean hospital stay was 1.8, ranging from 1 day to 10 day (Table No.3).

Reasons of Conversion in 550 cases

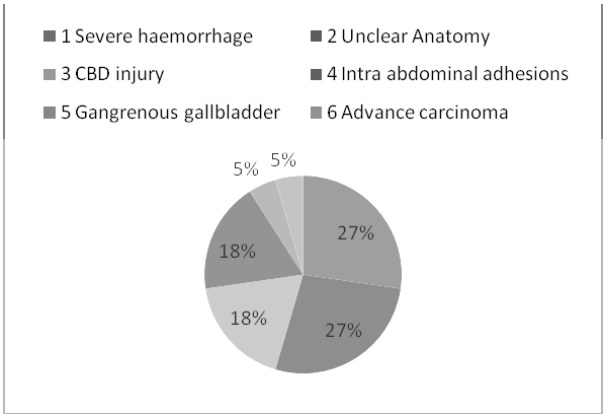
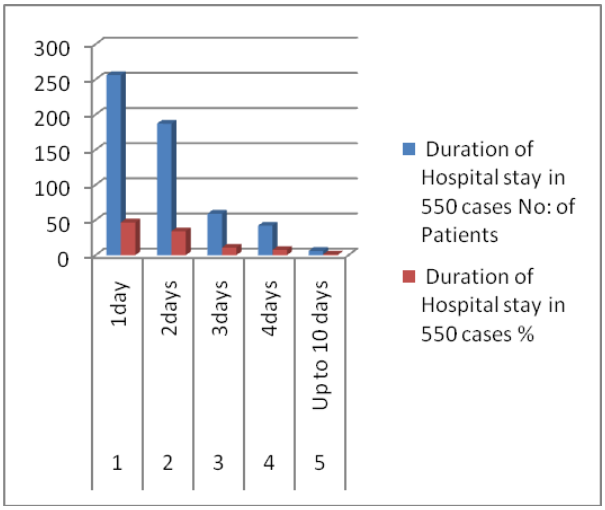


Table No.3: Duration of Hospital stay in 550 cases

Sr. No.	Duration	No: of Patients	Percentage %
1	1day	256	46.55
2	2days	187	34.05
3	3days	59	10.72
4	4days	42	7.59
5	Up to 10 days	6	1.09



DISCUSSION

Laparoscopic cholecystectomy has emerged as gold standard for laparoscopic procedures. The techniques are rapidly replacing traditional procedure. It is procedure of choice even in most difficult situations associated with complicated gall stone disease and on

the other hand it saves patients from ugly scar. There is less pain, less hospital stay and thus fewer burdens on hospital resources and saving of working hour2, 5, 7.initially there were many contra-indications for laparoscopic cholecystectomy but with increasing experience, there is no absolute contraindication. How ever in difficult cases, surgeon should always maintain low threshold for conversion into open procedure. The indication for conversion are controlled bleeding, injury to bile duct, inability to demonstrate the anatomy of region and severe adhesions [8-10]

In our study male to female ratio is 1:4.5. in various studies world wide the ratio varies from 1:3 to 1:11.5[11,12]. How ever predominance of female is obvious due to obvious reasons. In our study mean age is 47.63, while in literature it ranges from 40.5% to 52% [13,14]. The figures from the areas where early marriage occur mean age group is low. Our over all conversion rate is 4% while literature shows variation from 1.2% to 14% in different studies9-13. Common causes of conversion were unclear anatomy 6 (1.10%), intra-abdominal adhesion 4 (0.73%) how ever conversion rate in acute gall bladder disease was higher i-e acute cholecystitis 2 out of 22 (9.09%). In literature conversion rate in acute gall bladder disease has been reported up to 45% also[15,16].

Mean hospital stay in our study is 1.8 days while generally it ranges from 1.5 -3days in different series from literatures [17,18]. There was no mortality in our study, while in literature mortality reported ranges.

From 0% to 1.7%. Devil at al (1993) reports 0.04% mortality rate in 77604 patients from 4292 different centres13-15.There for we conclude that laparoscopic cholecystectomy has a gold standard procedure. It is safe and effective a becoming cost effective day by day. Incidence of complication is very low even less then open cholecystectomy. Morbidity and mortality are low. There is no absolute contra-indication for this procedure; however surgeon should have low threshold conversion especially in acute cholecystitis, bile duct injury, abscure anatomy, unmanageable adhesions and severe hemorrhage**.**

CONCLUSION

Laparoscopic cholecystectomy has a gold standard procedure. It is safe and effective and becoming cost effective day by day. Incidence of complication is low, morbidity and mortality are low. The pain free postoperative period and early ambulation lead to saving of value able working hours.

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Address for Corresponding Author:
Khush Muhammad Sohu,
Asstt. Prof., Dept. of Surgery,
GMMMC, Sukkur. Cell: 0300-3123854

Original Article

Comparison of Complications in Patients of Inferior Wall Myocardial Infarction with and without Right Ventricular Infarction

1. M. Zubair Zaffar 2. Abubakar Ali Saad 3. Bilal Ahsan Qureshi 4. Masood Iqbal Bhutta 5. Badar-ul-Ahad Gill 6. Sohail Saleemi

1. M.O. of Cardiology 2. Sen. Registrar of Cardiology 3. Assoc. Prof. of Cardiology 4. M.O. of Cardiology 5. Sen. Registrar of Cardiology 6. M.O. of Cardiology, Chaudary Pervez Elahi Institute of Cardiology, Multan

ABSTRACT

Objective: To compare in-hospital complications in terms of complete heart block and mortality in patients of inferior wall myocardial infarction with or without right ventricular infarction and to see the frequency of right ventricle infarction in patients of inferior wall myocardial infarction.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: The study was conducted at Chaudary Pervez Elahi Institute of Cardiology, Multan from 7th August 2009 to 6th February 2010.

Materials and Methods: 73 patients with inferior ST-segment elevation myocardial infarction were distributed into two groups; one with IWMI only and second with IWMI with RV infarction. Patients with prior MI, pre-existing heart failure, valvular heart disease, pericardial disease, acute pulmonary embolism, significant pulmonary diseases were excluded from the study. The data was analyzed by using software SPSS. The difference in frequencies of complications in two groups was compared using chi square test and a p value of < 0.05 was considered significant.

Results: Mean age was 51.95 ± 11.8 years in group 1 and 54.17 ± 12.0 years in group 2. Patients in group 2 had more complications as compared to group 1. The incidence of Complete AV block was 7 (38%) in group 2 vs. 6 (12%) in group 1. (p=<0.001).In-hospital mortality rate was 4 (23%) in group 2 vs. 3 (5%) in group 1 (p=<0.001).The incidence of right ventricular infarction in patients of inferior wall myocardial infarction was noted to be 26%.

Conclusion: RVI results in increase in the frequency of complete heart block and mortality in patients of inferior wall myocardial infarction with right ventricular infarction and the incidence of right ventricular infarction in inferior wall MI was 26%

Key Words: Inferior Wall MI, Right Ventricular Infarction, complete hear block, Mortality.

INTRODUCTION

Acute myocardial infarction (AMI) is the prototype of a real emergency. In fact, the most frequent complication of AMI is sudden death which still occurs within the first hour after symptoms onset[1]. Right ventricular infarction (RVI) complicates approximately 25% of acute inferior wall myocardial infarction (IWMI) [2]. Early recognition of RVI, namely by means of right sided electrocardiography (ECG) leads in acute IWMI has prognostic value[3]. RV infarction contributes markedly to hemodynamic instability, atrioventricular (AV) conduction blocks and in-hospital mortality in patients with inferior MI. Patients with inferior MI, who have RV infarction, appear to have a worse prognosis than those who don't have RV infarction.[4]

RVI diagnosis is based on clinical signs (hypotension and increased jugular venous pressure while pulmonary fields are clear), ECG (ST elevation by ≥ 1 mm in lead V4R), echocardiography and technetium pyrophosphate scanning. The clinical triad of hypotension, raised jugular venous pressure (JVP) and clear lung fields in patient with inferior MI is virtually pathognomonic for RV infarction.

The precordial ECG is the most readily available, simplest, objective, non-invasive and cost effective technique for diagnosing RV infarction.[5] ST segment elevations greater than or equal to 1 mm in leads V3R, V4R, V5R, and V6R is a reliable sign of right ventricular involvement. ST segment elevation greater than or equal to 1 mm in lead V4R was found to have the greatest sensitivity (93%) and predictive accuracy (93%). The diagnostic value of a QS pattern in lead V3R and V4R or ST elevation greater than or equal to 1 mm in lead V1 was much lower [6] . ST-segment depression in precordial leads has been associated with large infarction, worse wall motion abnormalities, lower ejection fraction and high short and long term complications and mortality.[7]

RV infarction can lead to serious complications. In-hospital complications were more in RVI i.e. cardiogenic shock, complete atrioventricular (AV) block, bradycardia and death.[8]It has been seen that patients with RV infarction have unfavorable prognosis. When IWMI is complicated by RVI, the in hospital mortality may be as high as 33% as compared to 3 % for patients of IWMI without RV infarct and incidence of RV infarct was 28%[9].

A study conducted by Khan et al revealed that RV infarction was found in approximately one-third of inferior MI patients and RV infarction was associated with considerable morbidity and mortality, and its presence defines a higher risk subgroup of patients with inferior wall infarction[10]. Complete atrioventricular (AV) block occurred in up to 42 % of patients of IWMI with RVI as compared to 29 % in patients of IWMI alone.[11]

This study was designed to see if RV infarction in patients with inferior MI increases the risk of in-hospital mortality and frequency of complete heart block.

MATERIALS AND METHODS

The study was conducted from 7 August 2009 to 6 February 2010 at Chaudary Pervez Elahi institute, in patients admitted to the emergency department with inferior ST-segment elevation myocardial infarction diagnosed by typical chest pain lasting more than 30 minutes but less than 24 hours, ST-segment elevation of ≥ 0.1 mV in two or more of leads II, III and aVF .Detailed history of the patient was taken and 12 lead ECG and right sided precordial leads was recorded. The patients were distributed into two groups.

- **Group 1:** It included patients with inferior wall MI only
- **Group 2:** It included patients of inferior wall MI associated with right ventricular infarction.

Patients were be followed by the researcher in emergency ward and coronary care unit (CCU) for up to 72 hours for the development of mentioned complications (complete AV block and in hospital mortality) through serial ECG and continuous ECG monitoring. All information was recorded on Proforma for each patient.

In-hospital outcome was studied in terms of following complications in patients of IWMI with and without RVI the development of complete heart block ,mortality.Patients of both genders with acute inferior ST-segment elevation MI, with and without RV infarction were included in this study having received the thrombolytic (streptokinase) therapy. Patients with prior MI, pre-existing heart failure, valvular heart disease, pericardial disease, acute pulmonary embolism,significant pulmonary diseases were excluded from the study.

The data was analyzed by using software SPSS 11. Numerical variables like age were presented as mean and standard deviation. Qualitative variables like gender, risk factors (DM, hypertension, smoking, hyperlipidemia, and family history of IHD) and complications (complete hear block and mortality) were presented as frequency and percentage.

The patients with inferior wall MI were compared with patients of inferior wall MI with right ventricular infarction for the mentioned complications. The two groups were compared using chi square test. A p value of ≤ 0.05 was considered significant.

RESULTS

The total study population (n=73) was divided into two groups. Group 1 comprised of patients with inferior wall MI only and group 2 comprised of patients of inferior wall MI with right ventricular infarction. Out of 73 patients, 54 (74%) were in group 1 and 19 (26%) were in group 2. There were 44 (81%) male and 10 (19%) female patients in group 1 and in group 2, there were 14 (76%) male and 5 (24%) female patients. The age in group 1 varied between 32-85 years (mean=54.91 ± 11.8) and in group 2, it was 35-80 years (mean=55.17 ± 12.0).

Table No.1: Distribution of Risk Factors Among Patients of Inferior MI With & Without RV Infarction

Risk Factor		IWMI (n=54)	IWMI + RVI (n=19)
Age (mean)		54.91 ± 11.8	55.17 ± 12.0
Sex	Male	43 (79%)	16 (83%)
	Female	11 (21%)	3 (17%)
Diabetes Mellitus		15 (29%)	6 (33%)
Hypertension		21 (39%)	10 (51%)
Smoking		31 (58%)	10 (51%)
Hyperlipidemia		4 (07%)	02 (10%)
Family History		14 (25%)	05 (29%)

Table No.2: In-Hopital Complications in Patients of Inferior MI with & without RVI

Complication	IWMI (n=54)	IWMI + RVI (n=19)	P value
Complete AV block	06 (12%)	07 (38%)	<0.001
Mortality	03 (05%)	04 (23%)	<0.001

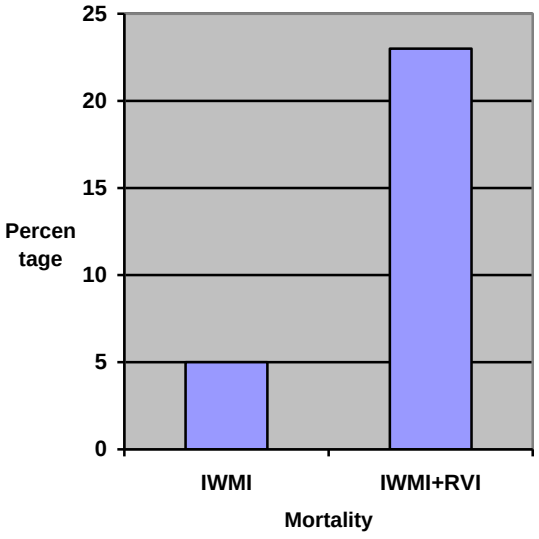

Figure No.1: Mortality in IWMI with and without RVI

The distribution of risk factors at presentation in group 1 (n=54) as compared to group 2 (n=19) was diabetes mellitus 15 (29%) vs. 6 (33%), hypertension 21 (39%) vs. 10 (51%), smoking 31 (58%) vs. 10 (50%), Hyperlipidemia 4 (7%) vs. 2 (10%) and family history 14 (25%) vs. 5 (29%). The prevalence of diabetes mellitus, hypertension, Hyperlipidemia and family history was higher in patients in group 2 while that of smoking was higher in group 1. (Table 1).

Regarding the incidence of complications, 7 (38%) patients in group 2 vs. 6 (12%) in group 1 suffered complete AV block (p=<0.001). In-hospital mortality was 4 (23%) deaths in group 2 vs. 3 (5%) in group 2 (p=<0.001), (Table 2). The major causes of death in group 2 were cardiogenic shock, AV blocks and ventricular arrhythmia.

DISCUSSION

The incidence of RV infarction can range from 10 to 50% as evidenced from previously conducted studies. The hemodynamic consequences associated with right ventricular infarction result in decreased pre-load and impaired atrioventricular conduction.

In this study patients with acute inferior wall myocardial infarction with right ventricular infarction had a relatively bad prognosis compared to those without right ventricular infarction. The presence of RV infarction is a strong indicator of in-hospital death and is associated with a higher incidence of complete AV block. These finding are consistent with studies by Zehender et al.[12]

The prevalence of RV infarction with inferior wall MI was 26% in this study as compared to prevalence of right ventricular infarction in study by Cintron et al.[13] Similarly right ventricular infarction was present in 32% patients in study by Zeymer et al by using electrocardiogrphic (ECG) criteria for diagnosis.[14] Piotr Kukla et al. reported an incidence RV infarction of 35.9% by using ECG criteria.[15]

Various studies conducted in Pakistan on inferior wall myocardial infarction and RV infarction showed incidence of 28% by Ali et al [9], incidence of 30% by Akber et al[16] and 34% by Khan et al.[10] A very high incidence of 97% of RV infarction in inferior wall MI was documented by Asano et al [17] by using dual energy single photon emission computed tomography (SPECT) with Thallium-99m pyrophosphate and Thallium-201.

In this study, mortality is considerably high in inferior wall MI with RV infarction group as compared to patients who have inferior wall MI only i.e. 23% vs. 5% (p=<0.001) (Figure 1). Zahender et al showed 31% mortality in patients with inferior wall MI with RV infarction as compared to 6% for those with inferior wall MI only.[12] Ali et al reported a mortality rate of 33.3% in patients with right ventricular infarction compared with 2.6% without right ventricle infarction in inferior wall MI.[11] The causes of death were cardiogenic shock, AV blocks and ventricular arrhythmias which was higher in RV infarction group.

The frequency of complete AV block was higher in inferior wall MI with RV infarction group than without RV infarction. In above two groups the incidence of complete AV block was 38% vs. 12% (p=<0.001) respectively. Samadikhah et al described incidence of arrhythmia and conduction disorders in acute inferior wall MI with RV infarction vs. inferior MI without RV infarction. Incidence of AV blocks was 36% vs. 25% in two groups respectively.[11] In a study, Malla et al showed incidence of sinus node dysfunction of 20% vs. 6% in two groups respectively. In this study, incidence of sinus bradycardia, AV dissociation and ventricular arrhythmia was not significant and no case of RBBB in inferior wall MI with RV infarction was recorded as compared to 3.5% cases in inferior wall MI only.

CONCLUSION

It can be concluded from this study that patients with inferior MI who also develop RV infarction are of older age group, more haemodynamically unstable and are at increased risk of morbidity and mortality.

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Address for Corresponding Author:
Dr. Abubakr Ali Saad,
Senior Registrar,
Cardiology Department, Abdali Road,
Multan.
cardiologistmic@gmail.com
Cell No.03006301326

Original Article

Physical and Microbiological Analysis of Water from Different Sources of Karachi

1. Nadeem ul Haq 2. Amin uddin Sheikh 3. Naveed Faraz 4. Rafiq Khanani

1 Asstt. Prof. of Biochemistry, LCMD, Karachi 2. Asstt. Prof. of Pathology, LCMD, Karachi 3. Asstt. Prof. of Biochemistry, BUMDC, Karachi 4. Prof. of Pathology, DUHS, Karachi

ABSTRACT

Objective: A number of diseases are caused by consuming water of poor quality. According to a community health study 30% of all reported cases of illnesses and 40 % of deaths in Pakistan are due to waterborne diseases. The purpose of the study was to i) to determine the physical quality and presence of total coliforms and Escherichia coli count and also ii) to compare the coliform and Escherichia coli bacteria in drinking water of different towns of Karachi with WHO 's recommended values.

Study Design: Retrospective Study.

Place and Duration of Study: This study was conducted in the Department of Biochemistry in collaboration with Department of Microbiology, Basic Medical Sciences Institute, Jinnah postgraduate Medical Centre Karachi during the period of June 2007 to February 2008.

Materials and Methods: Multiple water sample collected from 18 towns of Karachi by different sources like Piped water, Hand pumps, Mineral bottles and Filter plants. The 250 milliliters sample for microbiological analysis was collected to perform all the required analyses and to provide for any quality control need, split samples or repeat examination. Statistical Package for Social Science (SPSS version 11.0) used for data feeding and analysis. The results was given in the text as number and percentage for qualitative/categorical variables like E. Coli and Coliform and mean and standard deviation for quantitative variables like Physical parameters (pH, Temp, DO, Conductivity, TDS).

Results: The pH in tap water samples ranged between 6.8 to 7.6. Temperature recorded at spot ranged between 25-32 ^{o}c. The dissolved oxygen varied from 3.6 to 4.8 pm, its permissible limit is 4ppm. In 108 tap water samples MPN of coliform/100 ml water samples were < 10 in 21(19.4%) samples and > 10 in 87(80.6%) samples. Recovery of E. coli as indicator organisms of fecal pollution in different water samples were found.

Conclusion: During the drinking water quality assessment a wide range of pollutions were found and generated very useful baseline information on the current pollution status of supplied water to Karachi which indicates that Karachi is receiving highly polluted water.

Keywords: water pollution, physical, microbiological analysis, Karachi

INTRODUCTION

Human health depends on safe water more than any other thing. Basically the life of human is related to safe drinking water. Most of the problems in developing countries are mainly due to the lack of safe drinking water[1].Aquatic pollution in Pakistan is mainly due to increasing anthropogenic and agricultural activities, fast urbanization, rapid industrial development, poor sanitation system and unhygienic practices by general public. According to a community health study 30% of all reported cases of illnesses and 40 % of deaths in Pakistan are due to waterborne diseases. Poor quality of water human consumption may be either due to the presence of harmful bacteria and absence or excessive electrolyte concentration.[2]The presence of minerals in drinking water can have both good and bad consequence. Several minerals known to be beneficial and essential for human life, while other are toxic even in small amount**.** [3]Polluted water is a major cause of human diseases, misery and death. According to the World Health Organization (WHO) about 4 million children die every year as a result of diarrhea caused by waterborne infections. The bacteria most commonly found in polluted water are coliforms excreted by human beings. Improperly designed rural sanitary facilities also contribute to contamination of groundwater.[4]The scanty hospital's data indicating that a substantial proportion of morbidity in Pakistan is due to use of polluted water. Gastrointestinal infections resulting in diarrhea show high frequency among children as well as adults.[5]The pathogenic strains have been associated with several diseases including diarrhea, urinary tract infections and meningitis. [6] In developing countries, diarrheal diseases are often associated with infant and child deaths (Sobel et al. 2004).[7]Based on crude presumptive tests, Hunter *et al.* reported, that *Escherichia coli* is present within many of the drinking pools.[8] Escherichia coli (E. coli) is a member of fecal coliforms that contaminate the drinking water from human and animal fecal waste.[9] Water-washed route in which disease is associated with scarcity of water for personal hygiene are scabies, skin ulcer, and conjunctivitis and water-based route which involves parasites include schistosomiasis. [10]

The purpose of the study was to determine the physical quality and presence of total coliforms, sand Escherichia coli count and also to compare the coliform and Escherichia coli bacteria in drinking water of different towns of Karachi with WHO values.

MATERIALS AND METHODS

This study was conducted in the Department of Biochemistry in collaboration with Department of Microbiology, Basic Medical Sciences Institute, Jinnah postgraduate Medical Centre Karachi during the period of June 2007 to February 2008.Multiple Water sample collected from 18 towns of Karachi.1) Kamari 2) Baldia 3) SITE 4) Lyari 5) Sadar 6) Orangi 7) North-Nazimabad 8) Liaquatabad 9) Jamshed 10) New Karachi 11) Gulberg 12) Gulshan-e- Iqbal 13) Korangi 14) Shah Faisal 15) Landhi 16) Binqasim 17) Malir 18) Gadap.

Water collected by different sources: 1) Piped water. 2) Hand pumps. 3) Mineral bottles. 4) Filter plants.

For Physical Parameters: Drinking water samples were collected from the residential areas of all towns of Karachi region at consumers ends houses, apartments, schools, hospitals, hotels, pumping stations, masajid, private hydrants, bore water etc. One liter polyethylene acid resistant, washed rinsed with deionized water and dried bottles were used. Bottles were completely filled with the water samples and after noting the physical parameters, 5ml of (conc.) $HN0_3$ were added as preservative to adjust the pH < 2.0. Sample numbers with dates were marked. 250 milliliters sample for microbiological analysis was collected to perform all the required analyses and to provide for any quality control need, split samples or repeat examination.

For Microbiological Parameters: For collection, use heat-sterilized bottles containing a sufficient volume of sodium thiosulphate to neutralize the bactericidal effect of any chlorine or chloramines in the water. Each bottle of 250ml capacity should contain 0.1ml of a fresh 1.8% (w/v) aqueous solution of sodium thiosulphate. When collecting the sample, exercise extreme care to avoid contaminating it with bacteria from the environment. The water sample collected was cultured on following media: MacConkey broth, Brilliant green lactose bile broth, EMB agar.

Statistical Package for Social Science (SPSS version 11.0) was used for data feeding and analysis.The means and standard deviation of quantitative/ continuous variables according to sources of water was compared by Student's "t-test". In all statistical analysis, only p-values <0.05 was considered significant.

RESULTS

Table 1 show the comparison of mean values of physical parameters pH, temperature and dissolved oxygen in different sources of water supply in Karachi recommended by WHO. The pH in tap water samples showed neutral characteristics and within the permissible limits of WHO. Temperature recorded at spot ranged between 25-32 ºc. The dissolved oxygen was also measured and was in permissible limit of 4ppm. The pH in bore water samples was also within permissible limits of WHO. Temperature ranged between 25-32 ºc. The dissolved oxygen varied from 3.6 to 4.6 ppm and was within permissible limits of WHO. In tap water samples the specific conductivity was also measured on spot, its range from 375 to 550 mmho/cm. The conductivity of bore water ranged from 914 to 2387 mmho/cm and was higher as compare to WHO. The TDS concentration of bore water in all towns of Karachi was above 500 ppm and lower than excess limits i.e. 1000 ppm while it was significantly higher in bore water as compared to tap water. (P< 0.05)

Table No.1: Comparison of Physical and Biochemical Parameters in Tap, Bore Sources of Water, Filter Plant and Mineral Water in Karachi

Parameters	WHO VALUES	Sources of Water in Karachi				Filter plant (n=12)		Mineral Water (n=12)		P-Value
		Tap water (n=108)		Bore water (n=108)						
		Mean	±SEM	Mean	±SEM	Mean	±SEM	Mean	±SEM	
PH	6.5 - 8.5	7.33	±0.038	7.34	±0.038	7.42	±0.047	7.59	±0.055	0.151
Temperature	Not mentioned	30.95	±0.339	31.44	±0.215	29.20	±1.290	30.90	±0.450	0.102
DO	4 ppm	4.40	±0.075	4.24	±0.054	6.20	±0.280	5.71	±0.401	0.001
Conductivity	500µ mohs	474	±6.2	1656	±77.5	561	±348.5	391	±43.1	0.001
TDS	500 mg/l	291	±3.6	1085	±87.9	348	±43.4	262	±22.3	0.001

Table 2 show the degree of bacterial pollution in different water samples. In 108 tap water samples MPN of coliform/100 ml water samples were < 10 in 21(19.4%) samples and > 10 in 87(80.6%) samples. In 108 bore water samples MPN of coliform /100 ml water samples were < 10 in 32(29.6%) samples and > 10 in 76 (70.4%) samples. In 12 mineral water samples MPN of coliform/100 ml water samples were < 10 in 08 (66.7%) samples and > 10 in 05 (33.3%) samples. In 12 filter plants water samples MPN of coliform /100 ml water samples were < 10 in 07 (58.3%) and > 10 in 05 (41.6%) samples.

Table No. 2 Recovery of Bacterial Pollution in different Water samples of Karachi

Water samples	MPN of Coliform per 100 ml of water	
	<10	>10
Tap Water (n = 108)	21 (19.4%)	87 (80.6%)
Bore Water (n = 108)	32 (29.6%)	76 (70.4%)
Filter Plant (n = 12)	07 (58.3%)	05 (41.6%)
Mineral Water (n = 12)	08 (66.7%)	04 (33.3%)

Table 3 shows recovery of E. coli as indicator organisms of fecal pollution in different water samples. In 108 tap water samples MPN/100 ml were found 29 (26.9%) positive samples. In 108 bore water samples MPN/100 ml were found 25 (23.1 %) positive samples. In 12 filter plants water samples MPN/100 ml were found 04 (33.3%) positive samples. In 12 mineral water samples MPN/100 ml were found 03 (25%) positive samples

Table No. 3: Comparative Distribution of E-Coli in Different Sources of Water Samples in Karachi

Sources of water	Positive No.	%
Tap water (n=108)	29	26.9
Bore water (n=108)	25	23.1
Filter Plant (n=12)	4	33.3
Mineral Bottle (n=12)	3	25.0

DISCUSSION

This study was designed to determine the physical and biochemical parameters along with total coliform and E.coli in potable water from different sources of Karachi. Although no health based guideline is proposed for pH, eyes irritation and other skin disorders are associated with values of pH greater than 11.

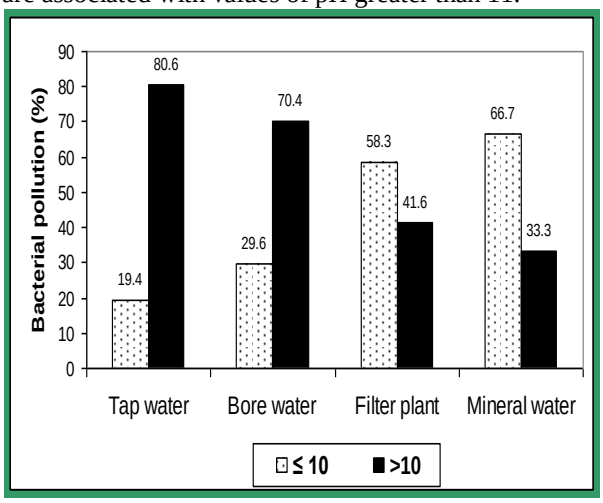

Figure No. 1:Recovery of Bacterial Pollution in different Water samples of Karachi

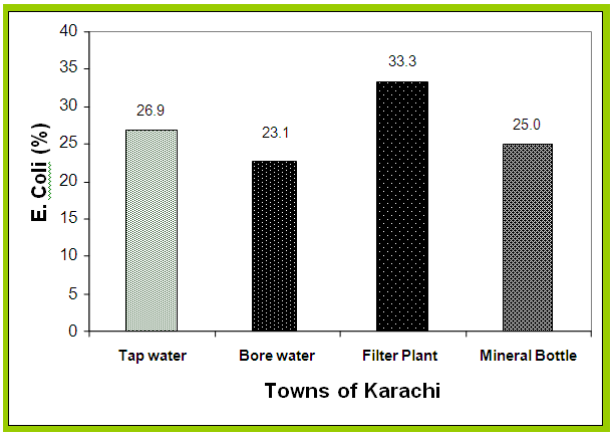

Figure No.- 2: Comparative distribution of e-coli in different sources of water samples in Karachi

The lower values of pH will also lead to the similar effect [11].In this study pH of both Tap and Bore water ranged from 6.8 to 7.6 were within the range of WHO (6.5-8.5) recommendations[12].The dissolve oxygen (DO) value is an index of pollution mainly due to organic matter. Usually ground water lacks dissolved oxygen so very low concentrations and support the growth of anaerobic microorganism[13]. Our study showed that dissolve oxygen were in the limit of 5 ppm from both sources.TDS in drinking water originate from natural sources, sewage, urban run-off, industrial wastewater, and chemicals used in the water treatment process and the nature of hardware used to convey water. In this study the conductivity in tap water of Orangi, Liyari, North-Nazimabad and Baldia towns were reported above 500 mmohs/cm and show disagreement, however the conductivity in other towns were within limit and showed agreement with WHO[12] recommended values. The water with a TDS level of less then 500 mg/l is consider to be good. The TDS test provides a measure

of the amount of dissolved ions but does not tell us about the nature of ions. [4] In this study the TDS of tap water was in accordance with the limit of 500 ppm, but the bore water concentration of TDS was not comparable and contained higher value than WHO[12] and were comparable with the results of Beg et al [14], Jaleel [15] and Mumtaz et al [16]. Agreement of our study were also found by Rehman et al who reported only 18% of total bore water samples contain TDS within permissible[17]

The absence of total coliforms, when used in conjunction with a source-to-tap multi-barrier approach, is used as part of the verification that the drinking water system is producing water that is microbiologically acceptable..Microbiological portability standards for drinking water in most developed counties relay on detection of total coliform and E- coli as marker of the human pathogen. The presence of coliform indicates that there is a high probability of other pathogenic organism. The poor bacterial quality of tap water in big cities has made bottled water popular in Pakistan. However the quality of most of the bottled water manufactured and sold in Pakistan is unsatisfactory both in chemically and bacteriologically [18].In this study we examined 240 water samples obtained from different sources. A total of 180(75%) samples were positive for presumptive test and showed complete agreement with Iqbal's study done in 1999 1n BMSI, JPMC,Karachi who showed 75% water samples positive presumption test for total coliform. Another study carried out in Uganda by Haruna et al[19] was in accordance with our study showed total coliform counts in 90% of the samples exceeded by WHO values.Our results showed disagreement with the Drinking Water Inspectorate of England and Wales that included in its regulations a mandatory value of zero coliforms per 100 mL in water leaving treatment works, a mandatory value of zero coliforms per 100 mL in 95% of samples for water in service reservoirs, and a non-mandatory value of zero coliforms per 100 mL at the consumer's tap. Analytical data showed that the drinking water in all over the 18 towns were very poor, and due to this reason many patients are visiting the hospitals daily, which were facing water born diseases.

CONCLUSION

Karachi receives water from Indus river and all major cities and industrial area also situated near the banks of Indus river, they are using water from Indus and discharge the waste water back into river without any treatment. The people of Karachi also using bore water because the shortage of municipal tap water. During the drinking water quality assessment water samples were collected and tested for wide range of pollution and generated very useful baseline information on the current pollution status of supplied water to Karachi.Our study concluded that Karachi is receiving highly polluted water.

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Address for Corresponding Author:
Amin-ud-Din Sheikh,
Assistant Prof. of Pathology,
Liaquat College of Medicine & Dentistry,
Karachi.
Cell No. 0347-2394401,
Email:aminuddinsheikh@gmail.com
House No 1-H-1/9, Nazimabad No.1,
Karachi 74600.

Original Article

To Study Therapeutic Effect and Benefit on Quality of Life in Scabies Patients

1. Farah Asad 2. Moosa Khan 3. Azam Samdani 4. Rafiqe Alam 5. Fatima Rizvi

1. M.Phil Student of Pharmacology, JPMC, Karachi 2. Asstt. Prof. of Pharmacology, JPMC, Karachi 3. Prof. of Dermatology, JPMC, Karachi 4. Prof. of Pharmacology, Karachi University, Karachi 5. M.Phil Student of Pharmacology, JPMC, Karachi.

ABSTRACT

Objective: To determine the quality of life by using 5% permethrin cream in scabies patients

Background: Scabies is a contagious, itchy ectoparasitic infection caused by sarcoptes scabiei mite. It is a common public health problem with an estimated global prevalence of 300 to 400 million cases. They increases day by day due to resistance/ recurrence and largely effect the quality of life of patients.5%permethrin is one of the effective treatment of scabies it is highly effective, well tolerated ,poorly absorbed and rapidly metabolized by skin.

Study Design: Open Label Clinical Trail study approved by ethics Committee of Jinnah Postgraduate Medical Centre, Karachi.

Place and Duration of Study: This study was conducted in Basic Medical Sciences Institute with Collaboration of Dermatology Department of JPMC, Karachi from 1st Dec 2010 to 30th Jan. 2011.

Materials and Methods: This study sample involved 65 clinically diagnosed scabies patients who were treated with 5% permethrin cream. Clinical data was collected by using questionnaire. Patients were divided into three age groups and given two applications of permethrin cream on first and 15 day. Follow up was done on Day 3, Day 15 and Day 30and there quality of life assessed using dermatological life quality index on day 0 and 30.

Results: It was found that quality of life in scabies patients was low and treatment with permethrin cream clinically improved the symptoms of patients and their quality of life significantly.

Conclusion: Scabies has a social stigma and the quality of life of patient get effected because of night itching and lack of sleep which improves significantly following proper local therapy.

Key Words: Scabies, 5% permethrin cream, quality of life.

INTRODUCTION

Scabies is a common parasitic infection caused by the mite sarcoptes scabiei variety hominis, an arthrobe of order acarina[1]. It has been known since ancient time like Napoleon who seems to have suffered from the itch[2].

The world wide prevalence has been estimated at about 300 million cases yearly, although it is common disease of children but occur in both sexes, at all ages, in all ethnic groups and at all socio-economic levels[3,4]. It is major public health problem in developing countries[5]. It is Common in HIV and immunocompromised diseases because of impaired immunity[6].

It has an impact on patient's quality of life[7]. Scabies is one of six major epidermal parasitic skin diseases (EPSD)[8].

Skin diseases pattern may vary with geographical location and environment conditions. In cities like Karachi with hot / humid climate, pollution overcrowding and lack of sanitation predisposes to a variety of dermatological diseases[9].

Due to lack of clinical diagnosis by the General physician and also prescription of inadequate or inappropriate medication has contributed to the spread and resistance to therapy[10]. When the patient do not respond to therapy for long time its seriously effects their working ability and quality of life[11]. There are variety of drugs for scabies treatment permethrin is one of the effective topical application with minimal systemic absorption(2%) it has given encouraging result as such it was chosen for therapeutic management[12,13]. It acts on voltage dependent Na-channel by extended opening causing depolarization prolongs resulting paralysis[14]

MATERIALS AND METHODS

Study design:

This was open label clinical trail approved by ethics Committee of Jinnah Postgraduate Medical Centre, Karachi conducted in Basic Medical Sciences Institute with Collaboration of Dermatology Department. Cases diagnosed by consultant dermatologist and were enrolled to participate in the trail. Detailed questionnaire was completed and inform written consent was taken from patient and their relatives. Patients willing to participate were screened by applying the inclusion and exclusion criteria. Patients were divided into 3 groups according to age.

Inclusion criteria included; 1) night Itching, 2)Diagnosed cases of scabies either gender, 3) Age above 5 years and below 70 years 4) Demonstration of burrows or presence of lesion of scabies at the classical sites and 5)History of similar illness in the family. Three or more criteria mentioned above made the patient eligible to include the study.

Exclusion criteria included pregnant/ lactating women, crusted scabies, patient who had received treatment during last 1 month, diabetics and patients with hepatic impairment or with dermatological, cardiovascular and neurological diseases.

Eligible subjects were assigned to apply 5% permethrin cream overnight (over 14 hours) and then repeated the application on day15. The quality of life index assessed on the first day of enrollment following which treatment was applied, they were examined on the 15 day and the application was re-applied and finally was examined, clinically reassessed for dermatological life quality index on day 30. Patients were advised to apply cream from head to toe. Standard instructions were given about the nature of the disease, mode of application of drugs, importance of treating all the family members and close contact and about wearing clothes and bedding in hot water. They advised not to use any antipruritic or any other topical medication which could effect the efficacy of the given treatment.

Clinical Cure rate evaluated by VAS scoring, and quality of life was assessed using Dermatology life quality index which is comprised of 10 items, giving sum score ranging between 0-30, it is focuses on six domains, including symptoms and feelings, daily activities, leisure, work and schooling, personal relationship and treatments. Dermatological life quality index is a useful score for clinical grading , grade I (0-1) means no effect, Grade-2 (2-5) means small, grade 3 (6-10) means moderate, grade 4 (11-20) means very large and grade 5 (21-30) means extremely large effect on patients life. The Dermatological life quality index (DLQI) used according to instruction given by Findlay and Khan for adults (1993) and Lewis-Jones and Finlay for children (1994)

Statistical analysis

Data were analyses using SPSS software, mean±SEM and Dermatological life quality index (DLQI).

RESULTS

A total of 65 patients were enrolled in group A and divided according to age into 3 groups, from 5-25years(A1) 24 patients, in 26-45 years(A2) 21 patients and in 46-70 years of age(A3) 20 patients were involved, the enrolled 65 patients M=22,F=43.Out of total subjects 11 had no family involvement/close contact .55(84.4%) of patients were clinically cured at the end of treatment. One patient did not turn up for follow up. The details are shown in table 1.

The mean±SEM DLQI score was assessed in this study on day 0 before treatment and on day 30 after the treatment using the Dermatology life Quality Index questionnaire for adult and children.

In group A1 (age 5-25 years) on day 0 Mean was18.2±0.64 which significantly improved to 2.3±1.08 on the evaluation on 30th day since the enrollment of the patient. In group A2 (age 26-45 years) on day 0 the Mean was 15.6±0.79 which improved to 2.1±1.16 on 30th day of study. In group A3 (age 46-70 years) on day 0 Mean was 12.0±0.64 which significantly improved on 30th day that was 1.9±1.06. The overall Mean for the entire patient involved irrespective of age group improved to 2.1±0.63 from 15.5±0.50 with .001p-value as shown in table2.

9 patients out of 65 did not improved and not cured clinically may be due to poor compliance or resistance.

Table No.1: General characteristics of scabies patients treated with 5% 5%Permethrin cream

Parameters	**Permethrin cream (n=65)**	
	No 0f patient (n)	Percent (%)
Age in years		
5-25	24	36.9
26-45	21	32.3
46-70	20	30.8
Gender		
Male	22	33.8
Female	43	66.2
Family members with scabies		
None	11	16.9
1-3	39	60.0
4-5	6	9.2
6 and above	9	13.8
History of contact		
Yes	7	10.8
No	58	89.2
Type of lesion		
Barrows	30	46.2
Barrows and Vesicles	35	53.8
Barrows, Vesicles and Papule	0	0.0

Table No.2: Dermatological life Quality index (DLQI) of scabies patients on Day-0 and Day-30 in Group A (5%Permethrin cream)

	Group A Permethrin Cream (n=65)		
	Mean ± SEM		P-value
Follow-up available	(n=64)		
Quality of life (DLQI Score)			
Day – 0	15.5 ± 0.50		0.001
Day – 30	2.1 ± 0.63		
Quality of life according to age groups			
5-25 years (n=24) A1	Day – 0	18.2 ± 0.64	0.001
	Day – 30	2.3 ± 1.08	
26-45 years (n=20) A2	Day – 0	15.6 ± 0.79	0.001
	Day – 30	2.1 ± 1.06	
46-70 years (n=20) A3	Day – 0	12.0 ± 0.64	0.001

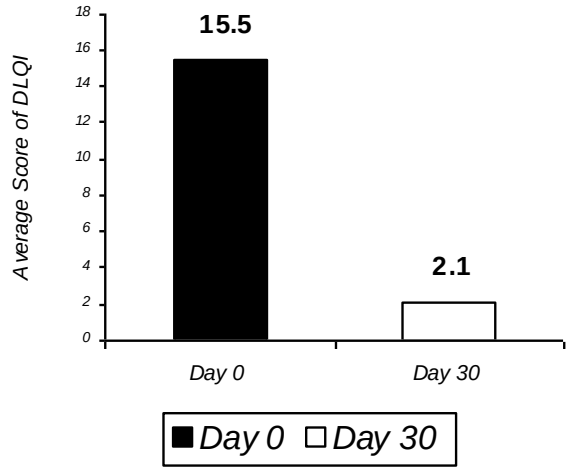

Figure No.1: Dermatological life Quality index in scabies patient on day 0 and day 30 in the treatment of 5% Permethrin cream

DISCUSSION

Health related Quality of life includes physical, functional, social and emotional well being of an individual[15]. The Dermatology life Quality Index (DLQI) may be used for routine clinical use for clinical evaluation, clinical decision making and research[16,17].

Scabies is a highly contagious disease. It is still major public health problem in many under develop countries in some of them are in an epidemic like situation it is common in over crowded, poor sanitation conditions and individuals with lack of hygiene[18,19]. Scabies also leads to social stigmas in certain societies, However quality of life has not been investigated in patient with scabies after treatment with permethrin although it largely effect the life style and working of individuals as shown in this study. However in one study sulphur has been used in the past and shown to cure the disease and in turn improving the quality of life[20].

There are many scabicides for the treatment of scabies how ever permethrin cream is considered one of the drug of choice for local application in its management[21]. Permethrin is one of the effective local therapy against scabies hence it was decided to use it in this study and monitor its effect on quality of life of patient using DQLI[22] one patient did not report for follow up and was dropped of the study. Total 64 patients were involved out of which 54 (84.4%) patients were cured thus indicating the efficacy of the drug on the all stages of mite (ova, larvae, and adult)[23]. Similar result has been reported with permethrin in an other study[24]. How ever our results were comparatively better then in the above study which was most probably due to the proper explanation regarding the local application of permethrin and the free samples provided to the patients/relatives for treatment. The mean of Dermatology Quality Life Index (DLQI) was 15.5±0.50 at day 0 in all the 64 patients involved in the study. The extensive degree of disease was effecting there quality of life which was significantly improved by treatment with 5% permethrin cream. Similar results with permethrin have been reported in the past in another study[25] with a some variations. Night time pruritus which is a hallmark feature of scabies is a severely unpleasant symptom impairing sleep and causing considerable reduction in health related quality of life especially during day time as evident from this study. Such results have been reported in another study[26, 27].

Permethrin was found to be effective and well tolerated, with no systemic effects and rapidly metabolized have been reported in the past[28,29]. The symptoms of scabies effects the quality of life of patients resulting in that deterioration of sexually, emotionally and psychologically features. The treatment of disease causes reversal and improvement of these symptoms[30].

CONCLUSION

The result of study suggest that Scabies largely effects the quality of life of patients. However treatment with 5% permethrin cream causes reversal of symptoms and brings the quality of life of the affected patients back to normal.

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Address for Corresponding Author:
Dr. Farah Asad
Dept of Pharmacology and Therapeutic,
Basic Medical Sciences Institute,
Jinnah Postgraduate Medical Centre, Karachi.
Cell No.0300-2533749

Original Article

Morphological and Immunofluorescent Patterns of Subepidermal Autoimmune Bullous Diseases of Skin in Karachi Pakistan

1. Shoaib Raza Rizvi 2. Saleem Sadiq 3. Saleem-ul-Haque

1. Sen. Lecturer, Sind Institute of Urology and Transplantation. Karachi 2. Prof. of Pathology, BMSI, JPMC, Karachi 3. Assoc. Prof. of Biochemistry, Avicenna Medical College, Lahore.

ABSTRACT

Introduction: Subepidermal autoimmune blistering disorders (SEABD) are common in dermatological practice. Direct immunoflourescence (DIF) staining is considered gold standard for the diagnosis of these disorders. This study was conducted to determine the morphological and DIF patterns of these disorders.

Study Design: Retrospective Study.

Place and Duration of Study: This study was conducted at the department of Pathology, Basic Medical sciences Institute, Jinnah Postgraduate Medical centre, Karachi, from January 2002 to July 2007.

Materials and Methods: Morphological and DIF patterns were recorded and categorical diagnoses of these disorders were established.

Results: Bullous pemphigoid (BP) was found to the most frequent disorder with a relative frequency of 60.71% and mean age of 54.82 years. Relative frequencies of childhood bullous pemphigoid (Ch BP), dermatitis herpetiformis (DH), chronic bullous dermatosis of childhood (CBDC) and herpes gestationis (HG) were 10.71%, 14.28%, 10.71% and 3.57% respectively.

Conclusion: Direct immunofluorescent staining is a one step procedure that should be done in all cases of SEABD. Use of salt split technique and immune electron microscopy would further enhance the level of certainty in SEABD.

Key words: subepidermal blister, direct immunofluorescent staining, bullous pemphigoid

INTRODUCTION

Subepidermal autoimmune blistering disorders are a heterogeneous group of disorders in which the blister is formed along the dermoepidermal junction. This group of diseases includes conditions with different clinical presentations, morphological findings and pathogenesis. Many bullous diseases look clinically identical, and clinicians rely heavily on morphological and in particular immunofluorescent patterns of these disorders[1]. Subepidermal autoimmune blistering disorders include bullous pemphigoid (BP), cicatricial pemphigoid (CP), linear IgA dermatosis (LAD), chronic bullous dermatosis of childhood (CBDC), herpes gestationis (HG), epidermolysis bullosa acquisita (EBA) and bullous systemic lupus erythematosus (bullous SLE)[2]. Pathogenetically they are characterized by the presence of antibodies directed against the structural components of dermoepidermal junction or basement membrane zone[3].

Immunoflourescence staining has become an indispensable tool in the diagnosis of autoimmune bullous diseases. In many cases, bullous diseases can not be differentiated clinically and needs the help of histopathological examination and immunoflourescence findings[4]. Direct immunofluorescent staining in particular is important in the diagnosis of SEABD[3]. Even in situation in which the histopathological finding seem characteristic of a specific bullous disease, DIF testing can add to the certainty of diagnosis, sometimes modify it, and occasionally reveals a different diagnosis[2].

Direct immunofluorescent staining is not widely available in Pakistan it is considered the "gold standard" for the diagnosis of autoimmune bullous disorders[5]. This study was planned to establish the morphological and immunofluorescent patterns of these bewildering disorders in our population.

MATERIALS AND METHODS

This was a retrospective study conducted at the department of Pathology, Basic Medical sciences Institute, Jinnah Postgraduate Medical centre, Karachi, from January 2002 to July 2007. All skin biopsies were reviewed and cases of bullous diseases were selected for detailed study. Paraffin blocks of SEABD cases were retrieved and DIF staining was performed on these cases, after the application of pronase as antigen retrieving solution. Panel of antibodies comprised of fluorescein isothiocyanate conjugate (FITC) labeled IgG, IgA, IgM, C3 and Fibrinogen. Slides were studied immediately under immunofluorescent microscope using scanner (4x), low power (10x) and high power (40x) objective lenses. Type, pattern, and location of deposition of various antibodies were recorded on the designed proforma and photographs were taken[6]. The definitive diagnosis was established with the help of morphological and immunofluorescent patterns of various cases. Different SAEBD were diagnosed according to criteria described in table 1[3]. Statistical

analysis was done using SPSS software. The results thus obtained were analyzed and compared with the results obtained from other locally and internationally published studies.

RESULT

A total of 62 cases of bullous disorders of skin were studied during the study period. Of these 34 cases belonged to intraepidermal bullous disorders and 28 cases of SEABD were found. Of the 28 cases of SEABD, there were 19 (67.85%) males and 9 (32.14%) females. The age ranged from 5-73 years. Morphological and DIF criteria, that was used for the categorization of various SEABD is shown in Table 1.

Table No.1: Morphological and DIF criteria for the categorical diagnosis of SEBD[3]

Diagnosis	Morphological features	DIF patterns
Bullous Pemphigoid	• Subepidermal bulla • Mixed inflammatory cells in blister cavity predominantly eosinophil • Festooning of dermal papillae	• Linear deposition of IgG ± C3 at the dermoepidermal junction
Dermatitis herpetiformis	▪ Subepidermal bulla ▪ ± Microabscesses at the tip of dermal papillae	• Granular deposition of IgA at the basement membrane zone
Chronic bullous dermatosis of childhood	▪ Subepidermal bulla Neutrophilic ± eosinophilic infiltrate at dermoepiderm	• Thick linear deposition of IgA at the basement membrane zone.
Herpes gestationis	▪ Subepidermal bulla ▪ Necrosis of basal keratinocytes ▪ Papillary dermal edema ± eosinophilic infiltrate	• Linear deposition of C3 ± IgG, IgM etc at the basement membrane zone.

In the present study BP had the lions share with 17/28 (60.71%) of cases. Old males were predominantly affected with a mean age of 54.82 years and 2.4:1 male to female ratio. Child hood Bullous pemphigoid (Ch BP) accounted for 3/28 (10.71%) cases. Mean age for this disorder in the present study was found to be 5.6 years.

Table No. 2: Various SEABD in the study (n=28)

Diag-nosis	No	%	Male	Female	Male to female ratio	Mean age
BP	17	60.71	12	05	2.4:1	54.82
Ch BP	03	10.71	03	-	-	05.66
CBDC	03	10.71	02	01	2:1	06.33
DH	04	14.28	02	02	1:1	21.50
HG	01	03.57	-	01	-	20.00

Key to table 2: (BP= bullous pemphigoid, Ch BP= childhood bullous pemphigoid, CBDC= chronic bullous dermatosis of childhood, DH= dermatitis herpetiformis, HG = herpes gestationis)

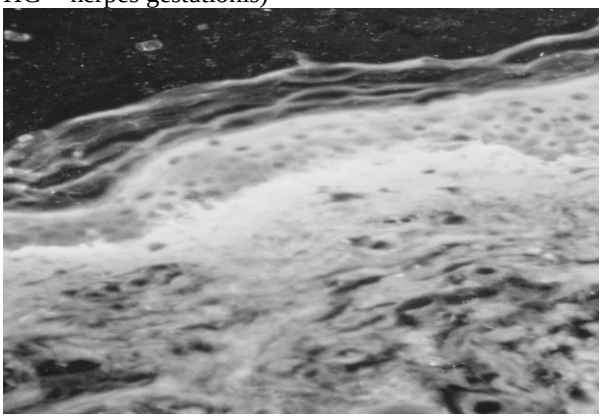

Figure No.1: Linear deposition of IgG at basement membrane zone in a case of bullous pemphigoid

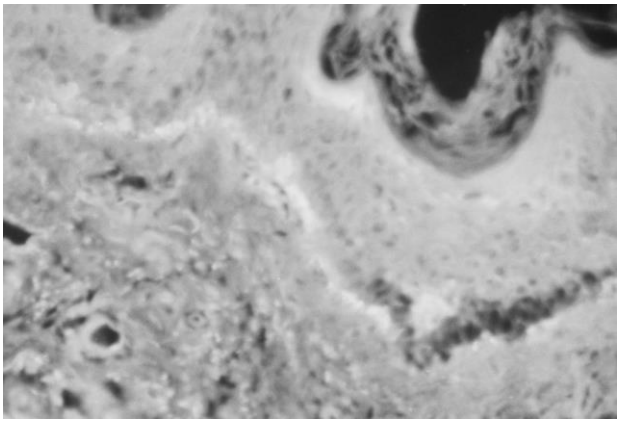

Figure 2: Granular deposition of IgA in a case of Dermatitis herpetiformis at dermoepidermal junction

All cases of BP (including Ch BP) showed subepidermal bullae with festooning of dermal papillae in 16/20 (80%) cases. Mixed inflammatory cell infiltrate predominantly eosinophil, neutrophil, lymphocytes and plasma cells was seen in all cases. Fibrin deposition was seen in 17/20 (85%) cases. Linear deposition of IgG was seen on DIF microscopy along with dermo-epidermal junction in 19/20 (95%) cases. Intensity of staining varied from + to +++. Linear deposition of C3 was also noted in 9/20 (45%) cases.

Diagnosis of DH was established in 4/28 (14.28%) cases. The age ranged from 3-50 years with a mean age of 21.50 years. Male to female ratio was 1:1. All cases of DH showed subepidermal bullae with formation of microabscesses at the tip of dermal papillae in 3/4 (75%) cases. Granular deposition of IgA was noted on DIF microscopy in all cases along basement membrane zone with additional deposition of C3 in 1/4 (25%) cases.

Mean age for 3/28 (10.71%) cases of CBDC was 6.33 years in our study with 2:1 male to female ratio. Subepidermal bulla with linear deposition of IgA along the basement membrane zone was noted in all the cases.

The only case that was diagnosed as HG showed a subepidermal bulla with concurrent history of pregnancy in a 20 years old lady. Presence of eosinophilic infiltrate and necrosis of basal keratinocytes was particularly noted. On DIF microscopy deposition of IgG, IgM and C3 was seen along the basement membrane zone in a linear pattern.

DISCUSSION

Although DIF is considered as the gold standard for the diagnosis of SEABD, it is not widely available in Pakistan[3]. An effort has been made through this study to describe the morphological and DIF patterns of these bewildering disorders.

Mean age for cases of BP in our study was slightly younger than that was described by Su and Ly in Hong Kong population. This relatively younger onset of BP in our study is supported by the hypothesis proposed by Su and Ly regarding the life style and life expectancy in Hong Kong population[7]. Although this finding is in accordance with the findings of Mehmood and Haroon, Mylowa et al and Adam BA[2,8,9]. Histopathological and DIF features are in accordance with those described by Fisler et al and Stern[10,11].

Mean age for the cases of DH was also younger in our study than described by Su and Ly[7]. This further augments the hypothesis proposed by Su and Ly[7]. Morphological and DIF features are compatible with the findings described by Williams et al and Browsi et al[12,13]. However DH is found in scattered age groups.

Morphological and DIF findings of CBDC in our series of patients were found to be identical as described by Navi et al and Kulthanan et al[16,15]. Mean age and male to female ratio were in accordance with those described by Peiying et al and Kulthanan et al[14,15].

Our morphological and DIF findings of HG are in accordance with the findings of Villegas et al[17]. However, there were not enough cases of DH, CBDC and HG, for any conclusion to be drawn.

CONCLUSION

DIF should be carried out in all the cases of SEABD in order to make the categorical diagnosis of these cases. Large population based studies using salt split technique and immune electron microscopy should be carried out to determine the nature of antibodies.

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Address for Corresponding Author:
Shoaib Raza Rizvi,
Senior Lecturer,
Sindh Institute of Urology and Transplantation.
Karachi

Original Article

Effect of Combined Oral Contraceptive Pills on Body Mass Index (BMI) in Women Attending Family Planning Centres, Karachi, Pakistan

1. Mamoona Shafiq 2. Saleem-ul-Haque 3. Hafeez-ul-Hassan 4. Sikandar Ali Sheikh

1. Asstt. Prof. of Physiology, IMC, Sialkot 2. Assoc. Prof. of Biochemistry, AMC, Lahore 3. Prof. of Physiology, BMC, Karachi 4. Prof. of Physiology, BMC, Karachi.

ABSTRACT

Objective: To see the effect of combined oral contraceptive pills on Body Mass Index (BMI) of women.
Study Design: A descriptive study.
Place and Duration of the Study: The study was conducted at Family Planning Centers at social obstetrical unit Baqai Medical University and Reproductive and Health Sciences (RHS) Institute, a family planning unit, at Jinnah Post Graduate Medical Center Karachi, from November 2010 to April 2011.
Subjects and Methods: This study was carried out on 50 patients of reproductive age 20-40 years. Patients with Cardiac, Renal and Liver dysfunction were excluded. Diabetic women taking sedative and hypnotics, anti-tubercular treatment were also excluded. All routine investigations were performed. BMI was done on initial visit re-evaluated after one, three & six months and data was analyzed.
Results: Fifty women were selected. They were divided into four categories, Control (category 0) i.e. before the start of COCPs, after 1 month (category 1), 3 months (category 2) and 6 months (category 3). On initial visit mean BMI of control is found to be 22.53 ± 1.92. Category 1 showed mean BMI of 22.53 ± 1.92 kg/m2 while BMI of category 2 is 22.53 ± 1.92 kg/m2 category 3 is 22.91 ± 1.87.
After completion of study mean increase in BMI of category 3 was 0.38 kg/m^2.
Conclusion: Mean increase in BMI of category 3 is negligible.
Key words: Combined oral contraceptive pills, Body mass index (BMI), Ethinyloestradiol, Levonorgestrel.

INTRODUCTION

The oral contraceptives were first approved for contraceptive use in the United States in 1960, and are a very popular form of birth control [1]. The leading method of contraception in the United States is the oral contraceptive pill, used by 11.6 million women. Usage of oral contraceptives varies widely by country, age, education, and marital status [2], currently used by more than 100 million women worldwide [3]. Awareness of family planning is widespread in Pakistan. According to a survey by Pakistan Status of Women and Fertility Survey (PSWFS) 2003 show a contraceptive prevalence rate of 32% [4]. According to a survey in Karachi, only 8% of women are using oral contraceptive pills [5].

Weight gain is often attributed as a side effect of combined oral contraceptive pills (i.e., an estrogen plus progesterone) use [6], and many women and clinicians believe that an association exists [7, 8, 9]. Concern about weight gain can discourage the initiation of combination contraceptive use and cause early discontinuation among users. Weight gain was the most frequently cited reason for oral contraceptive discontinuation in a national study of adult women in the United States [10]. Furthermore, even the perception of weight gain can lead to contraceptive discontinuation. Thus, concern about weight gain limits the use of a highly effective method of contraception.

Nevertheless, a causal relationship between combination contraceptives and weight gain has not been established. Several mechanisms by which combination contraceptives could lead to weight gain have been hypothesized. In general, adults tend to gain weight with age [11]. The weight gain is due to an increase in one or more factors: fluid retention, muscle mass and fat deposition. Fluid retention could be induced by the mineralocorticoid activity that occurs when ethinyl estradiol (E2), the estrogen in combination oral contraceptives, impacts the renin–angiotensin–aldosterone system [12]. Estrogen has been associated with increased subcutaneous fat, especially in the breasts, hips, and thighs [6]. The anabolic properties of combination contraceptives could result in increased food intake through a pharmacologic effect on satiety and appetite [13]. Alternatively, progestins could cause stress, anxiety, or depression, and these conditions, in turn, could be responsible for increased appetite and caloric consumption [6]. However, the most likely reason for the growing girth of women is a combination of genetic, environmental and lifestyle factors that have nothing to do with OC use [14].

In the clinical setting, simply weight measurement is insufficient; therefore one of the current recommended measures for weight gain and obesity is Body Mass Index [15]. BMI is defined as medical standard for obesity measurement and is employed by WHO obesity statistics. BMI is primarily a statistical tool designed for

public health study which enables the investigation & comparison of any medical data set in which the height and weights of subject are recorded, to determine whether obesity correlates with health outcomes. It was developed by Belgian Polymath Adoophe Quetlet in 1830-1850. It is calculated as follows. 2 BMI=Weight in Kg/Height in cm. Ideal normal range is 18.5 to 22.9 kg/m2 [16].

Detailed studies of the effect of combined hormonal contraceptives on weight gain have not been completed as it is difficult to control for factors such as caloric intake and activity level in women during long-term trials. In this study, we sought to investigate whether COCPs influence body weight in normal weight women while measuring BMI.

The reason of calculating BMI instead of weight is that BMI is the better indicator of total body fat & correlates more closely with adverse effects of excess weight than, body weight alone [16].

MATERIALS AND METHODS

The overall goal of this study was to determine if the use of COCPs has an effect on body weight. Two hundred & thirty women were attended in the hospital but only Sixty two met the inclusion criteria, out of which only 50 were followed till six months. Six of them were dropped from the study due to change of contraceptive method, four due to improper use of combined oral contraceptivve pills (COCPs) like missing one or more pills and two of them got pregnant so COCPs were discontinued.

Inclusion Criteria

- Women aged 20-40 years who were interested in contraception not desiring pregnancy for the duration of the study.
- Women with history of any or active uterine bleeding disorder like menorrhagia or polymenorrhea, to which other methods of contraception were not preferred.
- Carefully evaluated by clinical examination to be labeled as normal & healthy before starting the COCPs.
- Written or verbal consent was taken before enolment in the study.

Exclusion criteria

- Patients with hypertension & heart disease.
- Renal and hepatic dysfunction
- Diabetes mellitus
- The women not willing to take the COCPs.
- Patients who were already on COCPs.
- Post menopausal women.
- Women having Depot medroxyprogesterone acetate (DMPA) hormonal contraceptive injection in the past 90 days.

Obstetrical history was taken. General and systemic examination including Gyneacological examination was performed. A COCP with Ethinyloestradiol: 0.03mg, Levonorgestrel: 0.15mg was prescribed. The subjects were divided into four categories, Control (category 0) i.e. before the start of COCPs, after 1 month (category 1), 3 months (category 2) and 6 months (category 3).

Experimental Measures

Body weight and length: Body length was measured once at the beginning of the study. Body weight was measured after 1 month, 3 months and 6 months between 9 – 12 a.m.

Statistical Analysis

Compaison of BMI was done before and after the treatment by finding the means, calculating the standard deviation and standad error of mean. Student T- test was applied to check the difference between control and different categories BMI. Data has been analyzed using SPSS (version 10.0). Level of Significance $P < 0.05$.

RESULTS

Recipient age ranged from 22 to 36 years. Mean age was 28.8± 3.63. Height ranged from 150 to 163 cm with (mean 157.34 ± 3.99). On initial visit weight of the recipient in control group i.e. category 0 ranged from 44 to 65 kg, while BMI range was 17 to 26 kg/m^2 with mean BMI 22.53 ± 1.92. Category 1 showed mean BMI of 22.53 ± 1.92. On comparing control with category 1 non significant correlation (P>0.05) is observed.

The mean BMI of category 2 was 22.53 ± 1.92. Non significant (P>0.05) correlation was observed on comparison of control with category 2. While comparing control with category 3 still non significant

Table 1: BMI changes with pre and post Combined Oral Contraceptives administration

	Number (N)	**BMI** (kg/m^2) **Mean ± SEM**	**P value**
Control Category 0 (0 month)	50	22.53± 1.92	
Category 1 (1 month)	50	22.53± 1.92	P>0.05$^{\Delta}$
Category 2 (3 month)	50	22.53± 1.92	P>0.05$^{\Delta}$
Category 3 (6 month)	50	22.91± 1.87	P>0.05$^{\Delta}$

* P <0.05 S (Significant)
****** P <0.001 H.S (Highly significant)
Δ P >0.05 N.S. (Non significant)

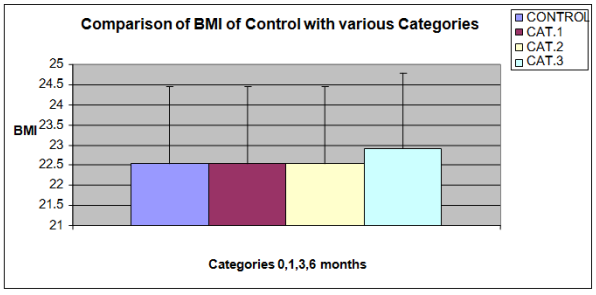

Figure 1: BMI changes with pre and post Combined Oral Contraceptives administration

(P>0.05) correlation is observed. It is due to very little rise in mean BMI which is 22.91 ± 1.87 (Table 1 & Figure 1).

After completion of study mean gain in weight was 1 kg while Mean increase in BMI was 0.38 kg/m^2.

DISCUSSION

Obesity is now recognized as a complex condition, resulting from interaction between genetic and environmental factors. In the clinical setting, simply weight measurement is insufficient; therefore one of the current recommended measures for obesity is Body Mass Index [15]. BMI is primarily a statistical tool designed for public health study which enables the investigation & comparison of any medical data set in which the height and weights of subject are recorded, to determine whether obesity correlates with health outcomes. Normal BMI range for females is 18.5 kg/m^2 to 22.9 kg/m^2. BMI < 18 kg/m^2 is under weight while BMI > 30 kg/m^2 is obese. Cut off values for Asian BMI for obesity is 27.5 Kg/m^2 [17].

Despite the popular notion that COCPs lead to weight gain, 42 randomized trials provided insufficient evidence to determine if COCPs have any effect on weight [18].

In general, adult female tend to gain weight with age [11]. However, the most likely reason for the growing girth of women in our population is a combination of genetic, environmental and lifestyle factors that have nothing to do with COCP use [14].

However, there are a number of studies with similar findings to our study demonstrating few Kg weight gain or no weight gain [19, 20].

Other researches on the use of steroid hormones during menopause have also been reported to cause no effects on body weight [21, 22, 23].

A study conducted in Thailand Based on field investigations of 391 married women aged 20 years or over, concluded that the use of contraceptive pills, which contain estrogen and progestin and were provided free of charge, tend to increase BMI [24].

Two studies showed mean weight gain greater than 2 kg as mentioned by Olerker et al [25] in 1995 and Endrikat et al [26] in 2001.

In our study small increase in weight may be due to an estrogenic effect which is responsible for increase in subcutaneous fat specially breast thighs and hips, and fluid retention due to Mineralocorticoid activity. Anabolic properties of COCPs could result in an increase in food intake due to its effect on satiety center [13].

CONCLUSION

Our study reveals that there is minimal effect of COCPs on BMI of the recipient. Weight gain is not an adverse effect of these preparations. Slight increase might be due to change in life style of the women using combined oral contraceptive pills. Misconception should be removed. Awareness should be promoted to continue COCPs.

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Address for Corresponding Author:
Dr. Mamoona Shafiq
Asstt. Prof. of Physiology,
Islam Medical College Sialkot.

Original Article

Evaluation of Protective Role of Benzodiazepine in Noise Stress Induced Activation of Hypothalamo-Pituitary Adrenal Axis in Albino Rats

1. Syed Meesam Iftekhar.H.Rizvi 2. Shoaib Raza Rizvi 3. Aftab Ahmed Sheikh 4. Saleem ul Haque

1. Asstt. Prof. of Anatomy, JM&DC, Karachi 2. Senior Instructor, Sind Institute of Urology, Karachi 3. Assoc. Prof. of Anatomy, LCM&D, Karachi 4. Assoc. Prof. of Biochemistry, Avicenna Medical College, Lahore.

ABSTRACT

Background: Noise, whether pleasant or not, is ever present in nature. Not much work can be done without noise; in the industries, fish market, social gatherings; it is constantly in the background. Though it seems harmless loud and or prolonged exposure to noise can cause health problems to the populace. Noise, as a recognized stressogenic factor, has been postulated to stimulate the HPA axis leading to the release of stress hormones.

Aims & Objectives: The present study was designed to assess the changes occurring in the level of stress hormones (ACTH & Corticosterone) in albino rats when acutely (24 hrs) exposed to loud noise with subsequent ameliorating effects of benzodiazepine (Valium/Diazepam) which will given to the rats to alleviate the symptoms of stress.

Study Design: Prospective Experimental Study.

Place and Duration of Study: This study was conducted in the Department of Anatomy, JPMC, Karachi from Jan 2006 to June 2008.

Material and Methods: Three groups of 10 rats labeled A, B and C serving as control (no noise), noise stress (24hrs) and noise stress (24hrs) with diazepam (5mg/kg) respectively. The groups B & C were exposed to white noise at 100dB. At the end of study the animals were sacrificed and their mean plasma concentration of ACTH and corticosterone were measured.

Results: A highly significant increase in mean plasma concentration of ACTH (150.90±14.71pg/ml) & corticosterone (5.72±0.28µg/dl) was observed in noise stressed group when compared with plasma ACTH (53.80±5.75pg/ml) & corticosterone (1.75±0.25µg/dl) concentration of control animals. This increase was significantly ameliorated by pre treatment of diazepam.

Conclusion: Our study shows the protective role of diazepam in stress induced by noise.

Key Words: Adrenocorticotropic hormone (ACTH), corticosterone, Noise stress, Diazepam, Hypothalamic-Pituitary Adrenal (HPA) axis.

INTRODUCTION

Stress is simply a fact of nature and an unavoidable consequence of life. Feeling of stress in humans results from interactions with the environment and is perceived as straining or exceeding their adaptive capacities, and threatening their well being.

Noise is a significant environmental problem [1] and has potential to cause stress reaction [2]. Pakistan is one country where urban sights and sounds resonate more with noise and air pollution than anything else. Air, water and noise pollution level in Pakistan is one of the highest in the world and is causing serious health concerns. According to a study conducted in 1994, noise levels from traffic in Lahore, Karachi, Hyderabad and Faisalabad range from 74-90dbA, 92-94dbA and 73-88dbA respectively. 6 places in Lahore, 7 places in Karachi, 6 places in Hyderabad and 2 places in Faisalabad were identified where the noise levels were greater than maximum permissible levels [3].

Noise level exceeding maximum permissible (60dB day & 50dB night) limits cause several physical ailments and social and emotional problems [4].

Noise, a stressogenic factor, causes disturbances in biochemical parameter of the body [5]. It acts as a physical stressor on animals that can lead to behavioral, physiological and anatomical responses [6]. Studies conducted on rats exposed to loud noise (85dB) have shown to stimulate HPA axis [7, 8].

Noise signals are sub cortically connected via the Amygdala to the Hypothalamic-Pituitary Adrenal (HPA) axis [9]. Studies using single label anterograde and retrograde tracing suggest limited evidence for direct connection between central or medial amygdale and paraventricular nucleus [10, 11, 12].

Noise, as a stressful stimulus is a widely accepted fact. However, an effective agent to counter the noise stress-induced biochemical alteration remains elusive.

Benzodiazepines are the class of drug that is widely prescribed mainly for their anxiolitic and sedative action especially for symptomatic relief of anxiety and tension states resulting from a stressful environmental or emotional factor [13]. As benzodiazepine can counteract the behavioral, neurochemical and hormonal modifications induced by stress, numerous studies have been focused on the role of benzodiazepine receptor in

response to stress. This is not only because of their anxiolitic, anticonvulsive, muscle relaxing and hypnotic properties due to direct action on the central nervous system, but also because of various effects both on non-neuronal tissues including Kidney, Lung, Heart, some endocrine glands and on several peripheral autonomic functions, such as gastric secretion, blood pressure and heart rate [14].

Diazepam, a classical benzodiazepine interacts with the benzodiazepine site of type-1 receptor complex, inhibits serotonin induce CRH secretion [15]. This reduction of CRH secretion leads to highly significant attenuation of the ACTH and cortisol increase following stress [16,17].

The present study was designed to assess the changes occurring in the level of stress hormones (ACTH & Corticosterone) in albino rats when acutely (24 hrs) exposed to loud noise with subsequent ameliorating effects of benzodiazepine (Valium/Diazepam) which will given to the rats to alleviate the symptoms of stress..

MATERIALS AND METHODS

Thirty normal, adult and healthy male albino rats of ages (90 - 120 days) weighing 220-350 grams were used. The animals were kept under observation for one week prior to the commencement of the experiment for assessment of their general state of health on the basis of weight gain or loss. Furthermore, this was also essential to acclimatize the animal to the environment of experimental room. All the animals were kept on standard laboratory diet and under closely controlled environmental conditions of 12 hour light / 12 hour dark cycle at room temperature.

All the animals were divided into three groups. The group A will serve as control, animals of group B were exposed to loud noise100 dB for 24 hours and received injection 0.9% normal saline intraperitoneally before the exposure to noise and the animals of group C were pretreated with inj diazepam (5mg/Kg) before exposure to loud noise 100 dB for 24 hours. The animals were sacrificed at the end of experimental procedure and all the experimental procedures were performed between 8:00 am to 12:00 pm in order to avoid circadian variations.

General appearance, i.e. activity, behavior and their food intake were checked daily.

Noise Stress Induction Procedure: Broad band noise (white noise) was produced by a white noise generator and amplified by an amplifier which was connected by loud speakers installed at a distance of 40cm at two opposite sides of the animal cage. The intensity of the sound was measured by precision sound level meter (TES -1351) Noise level was set at 100 dB uniformly through out the cages. The noise level of 100 dB is chosen because it is comparable with the noise level detected in discos, some industrial places and noise produce by some pressure horns used in most of the metropolitan cities of Pakistan.

Estimation of Plasma ACTH and Corticosterone Concentration: Blood samples were collected (by intra cardiac puncture) in tubes containing 10µl sodium EDTA and kept on ice until centrifuged. After centrifugation, the plasma was aliquoted and kept frozen at -70ºC until assay.

Plasma ACTH was measured by ACTH, RIA kit purchased from Immunotech, France. Standard acylated sample was added to ACTH antibody coated tube and then was incubated for 1 hour at room temperature with shaking. The assay sensitivity was 1.2pg/ml.

Plasma corticosterone was measured by rat corticosterone EIA kit purchased from Diagnostic System Laboratory, USA. The sample was diluted by using sample diluent and was added into antibody coated well, coated by polyclonal rabbit anti-corticosterone antibodies linked to inner surface of polystyrene well. Sample was mixed with enzyme conjugate solution. Then the plates (wells) were sealed and incubated for 24 hours. Later it was washed with wash solution for three times and tetra methyl benzidine was added to all wells and incubated for 30 minutes. Then 0.5 M HCl was added and sample was analyzed using micro plate reader. The assay sensitivity was1.6 ng/ml.

All the results were analyzed statistically by using SPSS version 12, by apply student t test.

RESULTS

Plasma ACTH concentration: Plasma ACTH concentration in various groups was analyzed by using radioimmunoassay kit. Their results and comparison of results are summarized in table 1 figure 1.

A highly significant increase ($P < 0.0001$) in mean plasma concentration of ACTH was observed in animals exposed to acute noise stress for 24hrs (150.90±14.71pg/ml) when compared with mean plasma concentration of ACTH in control animals (53.80±5.75pg/ml).

No significant change was observed in mean plasma ACTH concentration of animals exposed to 24hrs (acute) noise stress with diazepam (67.90±7.12pg/ml) when compared with mean plasma ACTH concentration of control animals clearly indicating the protective effect of diazepam in acute stress induced by noise.

Plasma Corticosterone Concentration: Plasma corticosterone concentration was analyzed in animals of various groups by enzyme immunoassay kit and their observation with comparisons are summarized in table 2, figure 2.

The mean plasma corticosterone concentration in animals exposed to 24 hrs (acute) noise stress was found to be 5.72±0.28µg/dl, which shows highly

significant increase (P <0.0001) when compared with mean plasma corticosterone concentration of control animals (1.75±0.25µg/dl).

Table No.1: Plasma ACTH Concentration pg/ml In Various Groups

Animal No	Control (A)	Acute Noise Stress (B)	Acute Noise Stress + Diazepam (C)
1	65	190	82
2	76	130	44
3	82	208	110
4	34	94	65
5	44	124	62
6	48	230	59
7	53	172	74
8	29	98	38
9	68	135	94
10	39	128	51
Mean	**53.8**	**150.9**	**67.9**
SEM	**5.75**	**14.71**	**7.12**

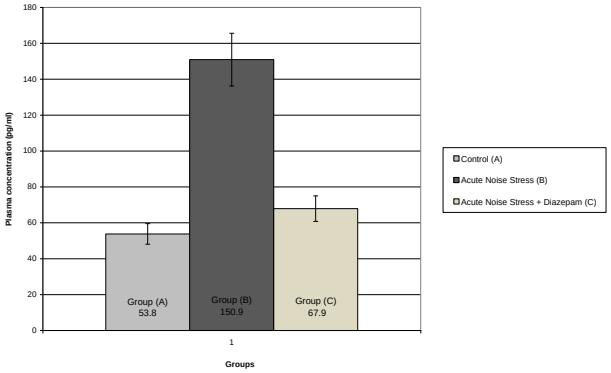

Figure No.1: Plasma ACTH Concentration (ph/ml) in various groups.

Table No.2: Plasma Corticosterone Concentration µg/dl in various Groups

Animal No	Control (A)	Acute Noise Stress (B)	Acute Noise Stress + Diazepam (C)
1	1.3	4.8	1.85
2	1.6	6.7	1.95
3	1.4	5.65	2.25
4	1.26	5.55	2.7
5	1.6	4.95	2.1
6	3.75	7.7	2.25
7	2.25	5.8	1.8
8	0.8	5.75	1.75
9	1.8	5.65	1.65
10	1.7	4.7	1.8
Mean	**1.746**	**5.725**	**2.01**
SEM	**0.25**	**0.29**	**0.1**

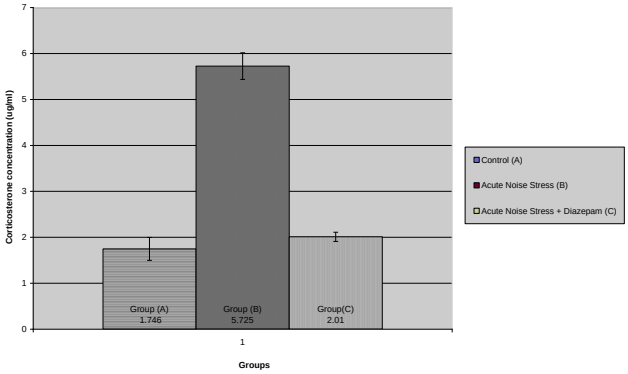

Figure No.2: Plasma Corticosterone concentration (ug/ml)

Insignificant change was observed in mean plasma corticosterone concentration of animals exposed to 24hrs (acute) noise stress with diazepam (2.01±0.1µg/dl) in comparison to mean plasma corticosterone concentration in control animal. This shows the protective role of diazepam in stress induced by noise.

DISCUSSION

Exposure of noise stress provokes cascade of reactions resulting in activation of HPA axis. Activation of HPA axis is the consequence of the convergence of stimulatory inputs from different region of brain into paraventricular nucleus of hypothalamus when the most important ACTH secreatougogues, corticotropin releasing hormone and arginine vasopressin are formed. Plasma levels of ACTH and corticosterone are considered as good marker of stress for three main reasons: (a)Their plasma levels are proportional to the intensity of emotional and systemic stressors, (b) daily repeated exposure to a stressor usually resulted in reduced ACTH response to the same stressor that is termed adaptation or habituation; (c) chronic exposure to stressful situations results in tonic changes in HPA axis that can be used as indices of the accumulative impact of these situations [18].

In our study we have observed the highly significant rise in plasma ACTH and corticosterone concentration when animals were exposed to acute noise stress. Our finding was found in agreement with the observation of Goshen et al., [19] ; Djordjevic et al., [20]; Liebseh et al.,[21] and Zheng and Ariizumi [22].

The Hypothalamus pituitary adrenal axis exerts a variety of effects at both the central and peripheral level. Its activity is mainly regulated by CRH, AVP, and Glucocorticoid.-mediated feedback action [23].

Numerous previous studies has shown that Benzodiazepines profoundly suppress the basal and stress related activation of HPA system and discontinuation of these drugs results in rebound activation[24]. Acute intra peritoneal administration of diazepam (2mg/Kg) inhibits the activity of the HPA axis, i.e., it decreases the concentration of Adreno-corticotropic hormone (ACTH) and corticosterone in female rats [25].

Benzodiazepine, possess a clear inhibitory influence on the activity of HPA axis in both animals and humans. This effect seems to be mediated at the hypothalamic and/ or supra hypothalamic levels via suppression of CRH [17,26,27]. A number of experimental studies clearly suggest that benzodiazepines attenuate the CRH secretion possibly through inhibitory GABAergic neurons [16,28].

In animals treated with diazepam before exposure to acute noise stress significant decrease in the plasma level of ACTH and corticosterone was observed. Several studies support our observations. Fukumistu et al., (2005)[29] found significantly lower serum corticosterone concentration in animals treated with diazepam (10mg/Kg) before subjected to psychological stress. Eisenberg [30] observed a significant protection of pretreatment of diazepam (5mg/Kg) from rise in plasma corticosterone concentration in animals exposed to sound vibration, a non invasive stress. According to Rohrer et al.,[16], administration of benzodiazepine led to a highly significant attenuation of ACTH increase following stress.

CONCLUSION

Our study shows the protective role of diazepam in stress induced by noise.

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Address for Corresponding Author:
Syed Meesam Iftekhar. H. Rizvi,
Asstt. Prof. of Anatomy,
Jinnah Medical & Dental College, Karachi.
B-256 Sector 11-B North Karachi,
Cell No: 0300-2076129
E-mail:i_m_meesam2004@yahoo.com

Original Article

Are Students of Isra University Sleep Deprived; A Prospective Study

1. Asmat Kamal Ansari 2. Aijaz Ahmed Qureshi 3. Abdul Hafeez Baloch

1. Prof. of Physiology, RMC, Peshawar 2. Assoc. Prof Physiology, SMC, Karachi 3. Assist Prof of Anatomy, Al-Tibri Medical College, Karachi.

ABSTRACT

Objectives: To assess the sleep pattern of students of Isra University using Pittsburgh sleep quality index &Epworth sleepiness scale.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at Isra University medical college Hyderabad Sind from Jan 2010 to June 2010.

Materials and Methods: One hundred medical students of various batches of Isra University were randomly selected for this study. There were 57 females & 43 males. All were given instructions to fill the questionnaires of Pittsburgh sleep quality index &Epworth sleepiness scale. These were then collected and analyzed.

Results: Among the students mean Epworth score was 8.37 $\pm$ .342 and the mean Pittsburgh score was 5.99 $\pm$ 0.322. Pittsburgh score was above the reference value. There was no difference in these scores between male & female students. In 34% students, Epworth score was above 9 and in 55% students Pittsburgh score was above 5. Both scores were higher in more female students than males. 26% students had less duration of sleep & 13% had difficulty in daily routine due to insufficient sleep.

Conclusion: It is concluded that Sleep as assessed by using Epworth sleepiness scale was within normal range. Mean Pittsburgh sleep quality index was above normal range indicating poor sleep quality. Duration of sleep was mainly affected.

Key Words: Pittsburgh score, Epworth score,

INTRODUCTION

Sleep is essential for health and quality of life.[1] Insomnia is a subjective complaint of dissatisfaction with the quantity, quality or timing of sleep. This disorder is estimated to occur in approximately 12% to 25% of the general population. [2, 3]

Sleep deprivation causes anxiety and many other health problems. It causes stress, proneness to accidents, mental illness and even premature deaths. [4]

College students suffer from more sleep disturbances than the general population. Sleep difficulties in college students can lead to lower levels of performance, memory, and cognitive ability, as well as increased levels of anxiety and decreased levels of well-being. Sleep quality is also highly correlated with college students' emotional response to stress. [5]

Gaultney JF (2010) reported from his study that Twenty-seven percent of students were at risk for at least one sleep disorder & those at risk may also be at risk for academic failure. [6]

Taylor DJ (2010) found that students get insufficient sleep and frequently use medication as sleep aids, use stimulants as alertness aids, and fall asleep at the wheel, or have motor vehicle accidents due to sleepiness [7]

It has been reported that short sleepers (6 hours or fewer in 24 hours) had an average GPA of 2.74 compared to longer sleepers (9 or more hours in 24 hours) with an average GPA of 3.24. Lack of sleep decreases students ability to concentrate and results in more errors in work. [8]

Buboltz, Brown, and Barlow (2001) observed that there was a high percentage of sleep problems in students, which supported past research that college students suffer more from sleep problems than the "normal" adult population.[9]

63% of college students do not get enough sleep, according to a recent study by the National Sleep Foundation. 15% percent of college students admit that they fall asleep in class. Students who studied hard all week and then stayed up all night partying on the weekend lost as much as 30% of what they had learned during the week. [10]

About 68 percent of college students who were surveyed said that worries about school and life keep them awake, with one-fifth saying this occurs at least once a week. It was found that less than a third of the 1,125 survey participants get the eight hours of sleep at night that people their age need. [11]

The ESS is a self-administered questionnaire with 8 questions. It provides a measure of a person's general level of daytime sleepiness, or their average sleep propensity in daily life. It has become the world standard method for making this assessment. [12]

The Pittsburgh sleep quality index (psqi) is designed to assess sleep quality during the past month and contains 19 self-rated questions from which 7 component scores are calculated and summed into a global score. Higher scores represent worse sleep quality: component scores

range from 0 to 3 and global scores range from 0 to 21[13].

Present study was undertaken to observe sleep problems in the students of Isra University Hyderabad Sind.

MATERIALS AND METHODS

Selection of subjects-

One hundred medical students were randomly selected from various classes of Isra University. These included students from all batches available, 57 female & 43 males.

After permission from ethical committee and informed consent from subjects, printed Performa with ESS and PSI were distributed among all subjects. Each performa contained instructions / guidelines for filling it.

Students taking drugs for sleep regularly, those with an apparent physical or psychological problem & those whose life pattern has recently changed were excluded from this study.

Data analysis

Properly filled performas were collected and two scales were evaluated as follows;

Pittsburgh Sleep Quality Index-

Answers of all questions were converted into seven components from C1 to C7. After determining score of each component, all seven were added. This was global Pittsburgh score.

Epworth Sleepiness Scale

This included the chances of dozing under various conditions.

Following scale were used to choose the most appropriate number for each situation:

0 = would never doze or sleep.
1 = slight chance of dozing or sleeping
2 = moderate chance of dozing or sleeping
3 = high chance of dozing or sleeping

RESULTS

The results are summarized in tables 1-5

Table No.1 shows mean sleep scores in all students. Mean Epworth score was 8.37 ± .342 & mean Pittsburgh score was 5.99 ± 0.322.

Table No. 2 shows Sex-wise comparison of two scores in all students. Mean Epworth score in males was 8.42 ± 0.346 & 8.30 ± 0.339 in females. There was no significant difference in Epworth score in two groups.

Mean Pittsburgh score in males was 5.98 ± 0.355 & 6.00 ± 0.290 in females. There was no significant difference in Epworth score in two groups.

Table No.3 shows sex wise individualPittsburgh sleep index score in all students. There was no difference in any component between two groups.

Table No.1: Mean Sleep scores in all students

Group	N	Epworth	Pittsburgh
students	100	8.37 ± .342	5.99 ± 0.322

Table No.2: Sex-wise comparison of two scores in all students

Scores	Male (n=45)	Female (n= 57)	P-value
Epworth	8.42 ± 0.346	8.30 ± 0.339	0.801
Pittsburgh	5.98 ± 0.355	6.00 ± 0.290	0.961

Table No.3: Sex wise individual Pittsburgh sleep index score in all students

Component	Component Score	
	Male	Female
C1	.87	.58
C2	1.22	1.25
C3	1.62	1.84
C4	.02	.02
C5	.91	.95
C6	.11	.09
C7	1.44	1.19

Table No.4: Subjects with Epworth score more than 9

Epworth score	Males	Females	Percentage
>09	13	21	34

Table No.5: Subjects with Pittsburgh score more than 5

Pittsburgh score	Males	Females	Percentage
>05	22	33	55

Table No.6: Subjects with Pittsburgh sleep index 03 in various components

Component	Total Students	Male	Female
C1-subjective sleep	04	03	01
C2-sleep latency	05	01	04
C3-sleep duration	26	09	17
C4- habitual sleep efficiency	00	-	-
C5-sleep disturbances	00	-	-
C6- use of medicine	00	-	-
C7-day time dysfunction	13	08	05

Table No.4 shows subjects with Epworth score more than 9. This included 13 males & 21 females. Over all 34% of students had Epworth score above 9.

Table No.5 shows subjects with Pittsburgh score more than 5. This included 22 males & 33 females. Over all 55% of students had Pittsburgh score above 5.

Table No.6 shows subjects with Pittsburgh sleep index 03 in various components. 26% of the students had C3 component value of 03 and 13% of the students had C7 component score of 03.

DISCUSSION

College students suffer from more sleep disturbances than the general population. This has been reported by various previous studies [5, 6, 7, 8, 9, 10, 11, and 12].

In the present study, one hundred medical students were randomly selected from various batches of Isra University; 57 females & 43 males. Their sleep pattern was evaluated by using Epworth & Pittsburgh sleep scales.

In our study, mean Epworth score was 8.37 ± .342. General reference value of this score is between 0-9 (12) while normal range in Australia is 4.6, in USA 4.5 and in Italy 4.4. [14]. we found no significant difference in Epworth score between males and females staff members. Previous studies have also not shown any gender difference in this score. [14]

The Epworth Sleepiness Scale (ESS) measures the daytime sleepiness and has been found to be normal in many people with a variety of sleep disorders. About 10 – 20 percent of the general population has ESS scores > 10 [14]. The ASP is not synonymous with fatigue or tiredness. Although the students complain of too less sleep, their ESS was within normal limits but on the higher side.

In our study, mean Pittsburgh sleep quality index (psqi) was 5.99 ± 0.322.A global score of 5 or more indicates poor sleep quality; the higher the score, the worse the quality. [15] So, this score in our students indicates poor sleep quality & quantity. When compared, we found no significant difference in this score or any of its componentsbetween males & females.

When we analyzed scores of different individuals, we found that 34% of the students had an Epworth score more than 9. These included 21 females & 13 males. Similarly, 55% of students had a Pittsburgh score more than 5. These included 33 females & 22 males. This reveals that sleep problem was more frequent in female students than in males. Previous studies also reveal that female students suffer more from sleep disturbances than males. [9]

Analysis of individual components of Pittsburgh sleep index reveals that 26% of the students had value of C3 of 03. This component indicates duration of sleep. So, most common sleep problem in this study was insufficient sleep duration. Similarly, 13% students had component C7 of 03 values. This component indicates daytime dysfunction. So these students had difficulty in their routine daily work due to insufficient sleep. Also some students had difficulty in going to sleep with their C2 value of 03.

Gaultney JF (2010) in his study of 1,845 college students found that Twenty-seven percent of students were at risk for at least one sleep disorder. They were also at the risk of academic failure. [6]

Stress about school and life keeps 68 percent of students awake at night - 20 percent of them at least once a week. The study of 1,125 students appears online in the Journal of Adolescent Health. It found that only 30 percent of students sleep at least eight hours a night — the average requirement for young adults. [11]

Sleep is a very important component of a person's life, and its potential effects should not be overlooked. There are many studies that suggested that sleepiness & lack of sleep can adversely affect the academic performance of the college students. [16, 17, 18, 19].

Therefore, this sleep problem in students of our university should be taken seriously and its solution be sorted out.

CONCLUSION

It is concluded that Sleep as assessed by using Epworth sleepiness scale was within normal range. Mean Pittsburgh sleep quality index was above normal range indicating poor sleep quality. Duration of sleep was mainly affected.

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Address for Corresponding Author:
Prof. Dr. Asmat Kamal Ansari,
Deptt. of Physiology,
Rehman Medical College, Peshawar.
Cell: 0300-3041293

Original Article

Susceptibility Pattern of Pathogens Isolated from the Prostatic Tissue

1. Rizwana Barakzai 2. Saleem A. Kharal 3. Shaheen Akbar Agha 4. Samina Rizvi 5. Sajjad Shaikh 6. Muhammad Akbar Agha 7. Aamir Mirza

1. Asstt Prof of Pathology, SMC, DUHS, Karachi 2. Prof. of Microbiology, BMSI, JPMC, Karachi 3. Assoc. Prof. of Community Medicine, SMC, DUHS, Karachi 4. Asstt. Prof. of Pathology, SMC, DUHS, Karachi 5. Assoc. Prof. of Pathology, KM&DC, Karachi 6. Prof. of Pathology, DIMC, DUHS, Karachi 7. Asstt. Prof. of Microbiology, DIMC, DUHS, Karachi.

ABSTRACT

Background: There is significant incidence of bacterial growth in the prostatic tissue in the patients with Benign Prostatic Hyperplasia (BPH), whereas pre-existing urinary tract infection is not a reliable indicator by which this group can be identified pre-operatively and prostatic infection could be treated.

Objective: To identify the presence of various types of bacteria and fungi in prostatic tissue and cultures from urine samples of patients undergoing transurethral resection of prostrate

Study Design: Cross-sectional observational study design.

Place and Duration of Study: This study was conducted at The Basic Medical Science Institute at Jinnah Postgraduate Medical Center (JPMC) Department of Microbiology Karachi from .

Material and Methods: The samples were processed by the standard protocol. Culture medium of Blood agar and MacConkeys agar were used and biochemical tests were performed by using different sugar media, triple sugar iron agar, Simon citrate agar, urease, indole and MRVP tests.

Result: Out of 100 cases 25% cases showed identical type of growth, 11% cases had different type of growth in urine and prostatic tissue culture whereas 5% had no growth in urine while 32% had no growth in prostate only 32% had no growth in both urine and tissue culture.

Conclusion: The significance of prostatic tissue culture of patients undergoing surgery facilitates prompt diagnosis and the ideal choice of antibiotic can shorten the duration of treatment.

Keywords: Benign Prostatic Hyperplasia (BPH), Lower Urinary Tract symptoms (LUTS) , transurethral resection of Prostate(TURP).

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the nonmalignant enlargement of the prostate gland. The prevalence of Lower Urinary Tract symptoms (LUTS) due to BPH increases with increasing age. Moderate to severe symptoms occur in 40 and 80% of men after the age 60 and by 80 years, respectively. Nearly all men develop microscopic BPH by the age of 90.[1]

The Recurrent urinary tract infections, like upper urinary tract infections are also the cause of morbidity.[2] the risk of antibiotic-resistant organisms is increased. Therefore, preventing the occurrence of antibiotic-resistant organisms through the use of suitable antibiotics is a major issue.[2]

Bacteriuria is much more prevalent among elderly population than it is among young adults. Catheter related urinary tract infection accounts for 40% of nosocomial infections, urinary tract infection is the complication of long term urinary catheterization.[3]

E. coli ,is the most common organism causing bacteriuria in catheterized patients and there is a significant association between periurethral colonization and subsequent bactiuria.[4]

Obstruction may develop because the bacterial glycocalyx, the slime layer biofilm that some bacteria produce coat the surfaces of the catheter. It encourages the formation of encrustations and infection stones consisting of urea, mucoprotein and other complex substances .[5]

The presence of bacteria was demonstrated in significant number of patients undergoing prostatectomy for benign prostatic hyperplasia. The micro-organism most frequently isolated in the quantitative bacterial cultures were, by order of frequency, coagulase negative Staphylococci, Escheriachia coli and Enterococcus faecalis (Soler et al., 1999).[6]

Catheter-related recurrent UTIs require multiple courses of antibiotic therapy. Eventually, the risk of antibiotic resistant organisms is increased. Therefore, to prevent the occurrence of antibiotic-resistant organisms the use of suitable antibiotics is a major issue.[7]

The study was conducted to isolate the bacteria from the urine and prostatic tissue obtained by TURP, to compare the frequency of the micro-organisms present in urine and prostatic tissue in catheterized and non-catheterized patients.

MATERIALS AND METHODS

One hundred samples of prostatic tissue and urine of the same patients were collected mainly from the department of Urology, Jinnah, PG. Medical Center, Karachi.

Among them, 50 patients had indwelling catheter for more than 20 days whereas 50 patients were non-catheterized. In present study none of the patients were on antimicrobial therapy at least 7 days prior to the collection of specimens.

The patients consent and demographic data was recorded and assessed in accordance with the International Prostate Symptom Score (IPSS). The IPSS is an eight-question written screening tool to rapidly diagnose BPH, track the symptoms of BPH and suggest management of the symptoms of BPH.[8, 9]

The samples were processed. Inoculation of uncentrifuged urine specimen was done with a calibrated (0.001 ml) wire loop on blood agar plates (BAP), MacConkey's and Sabourauds Dextrose agar plates of 9 cm (4 inches) diameters. These plates were incubated at 37°C for 24 hours. Number of colonies on the following day, were counted on the BAP. Cultural characteristics of the positive culture were observed and recorded. Gram positive organisms were further differentiated by doing catalase and coagulase test while bile esculin test was done to identify enterococci. Gram negative bacteria were separated by oxidase test and motility test. Lactose fermenters and non-lactose fermenter organisms were further identified by biochemical reaction after 24-48 hours. The same procedure was followed for the prostatic tissue which was received after TURP. The prostatic tissue was initially washed with sterilized saline and homogenized in sterilized mortar and pestle containing 1 ml saline.

RESULTS

Out of the 100 patients assessed 50 were catheterized and 50 were non-catheterized. The numbers of bacteria isolated in prostatic tissue of catheterized and non-catheterized patients are represented in Table 1 and numbers of bacteria isolated in urine of catheterized and non-catheterized patients are presented in Table2. The infection in the urine was present in 40 patients of which 29 were catheterized and 11 were non-catheterized and the infection in the prostatic tissue was present in 68 patients of which 42 were catheterized and 26 were non-catheterized (P value = 0.001 highly significant).

Out of 68 patients with positive culture in prostate 25 showed similar growth in both urine and prostatic tissue culture. Whereas out of 43 patients with positive culture in the prostate, eleven showed different organisms in urine and prostatic tissue and 32 patients had positive culture only in the prostatic tissue and no growth in the urine culture.

Organism isolated in urine and prostate of catheterized patient is shown in

table 3 and organism isolated in urine and prostatic tissue of non-catheterized patients is shown in Table 4.

Organism in the prostate of catheterized group were E.coli (23%) (8 OF 42), C.N Staphylococci 19% (8 of 42), Streptococcous faecalis 14% (6 of 42), Pseudomonas 11.9% (5 of 42), Proteus 6% (3 of 42), Serretia 4.8% (2 of 42), Providencia 4.8% (2 of 42), Enterobacter 7.1% (3 of 42), Salmonella 2.9% (1 of 42)

Organism in the prostatic tissue of non-catheterized patients was Streptococcus faecalis 27% (7 of 26), C.N. Staphulococci 23% (6 of 26), E.coli 15% (4 of 26), Citrobacter 7.7% (2 of 26), Providencia 3.8% (1 of 26), Salmonella 3.8% (1 of 26).

Table No.1: Bacterial Growth From Urine And Prostatic Tissue In Patients Under- Going Turp

Specimen	No. tested	Positive culture
Urine	100	40
Prostatic tissue	100	68

Table No.2: Organisms Isolated From The Prostatic Tissue In Patients With Bacterial Prostatitis Undergoing Turp

Organisms	Positive culture	Percentage
E.coli	14	20.59
C.N. Staphylococci	14	20.59
Streptococcus fecalis	13	19.12
Pseudomonas	06	8.82
Enterobacter species	06	8.82
Citrobacter species	04	5.88
Proteus species	03	4.41
Serretia marcesens	02	2.94
Salmonella species	02	2.94
Klebsiella species	01	1.47
Total	**68**	**100.00**

Table No.3: comparison of bacterial isolates from urine and prostatic Tissue of patients with bacterial prostatitis

Organisms	Positive Culture		Probability
	Urine (n=68)	Prostatic tissue (n=68)	
C.N. Staphylococci	10 (25.0)	14(20.6)	>0.594
Streptococcus fecalis	04 (10.0)	13 (19.1)	<0.209
E.coli	13 (32.5)	14 (20.6)	>0.167
Pseudomonas species	02 (5.0)	06 (8.8)	<0.464
Serretia marcesens	02 (5.0)	02 (2.9)	>0.584
Proteus species	02 (5.0)	03 (4.4)	>0.888
Enterobacter species	02 (5.0)	06 (8.8)	<0.464
Providencia species	00	03 (4.4)	>0.178
Citrobacter species	02 (5.0)	04 (5.9)	>0.845
Klebsiella species	02 (5.0)	01 (1.5)	>0.354
Salmonella species	00	01 (1.5)	>0.440

Urine culture showed high rate of bacteriuria in catheterized patient i.e. 73% catheterized patients (29 of

40) had positive culture reports of their urine, while 27% non-catheterized patients (11 of 40) had positive culture of urine samples. Most common organism isolated were E.coli 37.93% (11 of 39) and C.N. Staphylococci 27.5% of (8 of 29), Streptococcus faecalis was 13.7% (4 of 29), Serretia and Citrobacter were 6.8% (2 of 29) each while Klebsiella, Proteus and Pseudomonas were 3.4% (1 of 29) each and was also seen in 3.4% (1 of 29) each and was also seen in 3.4% (1 of 29) cases. Organisms difference in urine and prostatic were statistically not significant.

In non-catheterized patients bacteriuria was present in 27% of cases i.e. (11 of 40) had positive urine cultures and the most common organism were E.coli, Enterococci and coagulase negative Staphylococci 20% each i.e. (2 of 10) cases while Streptococcus faecalis, Pseudomonas, Citrobacter and Klebsiella were 10% (1 of 10) cases each, Serretia, Proteus and salmonella were absent in the urine of the non-catheterized patients.

Table No.4: Infection in Prostatic Tissue

Group	Present (68)		Not present (32)	
	No.	%	No.	%
Catheterized	42	61.80	08	25.00
Non-catheterized	26	38.20	24	75.00

P value = 0.001 (Highly significant)

Table No.5: Susceptibility Pattern of Major Pathogens Isolated From Urine

Antibiotics	Coagulase –ve Staphylococcus (n=10)	E.coli (n=13)	Streptococcus (n=4)	Pseudomonas (n=2)	Enterobacter (n=2)	Citrobacter (n=2)
Norfloxacin	07 (70%)	10 (77%)	02 (50%)	02 (100%)	01 (50%)	02 (100%)
Pipemidic Acid	08 (80%)	07 (54%)	01 (25%)	00 (00%)	01 (50%)	00 (00%)
Sparfloxacin	07 (70%)	09 (69%)	02 (50%)	01 (50%)	01 (50%)	02 (100%)
Trimethoprim	06 (60%)	05 (38%)	00 (00%)	00 (00%)	00 (00%)	01 (50%)
Trimethoprim + Sulfamethoxazole	08 (80%)	09 (69%)	00 (00%)	01 (50%)	01 (50%)	02 (100%)

Table No. 6: Susceptibility Pattern of Major Pathogens Isolated From Prostat Tissue

Antibiotics	Coagulase –ve Staphylococcus (n=14)	E.coli (n=14)	Streptococcus (n=13)	Pseudomonas (n=6)	Enterobacter (n=6)	Citrobacter (n=4)
Amikacin	11 (79%)	11 (79%)	10 (77%)	04 (67%)	04 (67%)	02 (50%)
Ampicillin	06 (43%)	03 (23%)	10 (77%)	00 (00%)	01 (17%)	01 (25%)
Ceftriaxone	12 (86%)	12 (86%)	09 (69%)	03 (50%)	05 (83%)	03 (75%)
Enoxacin	10 (71%)	10 (71%)	07 (54%)	04 (67%)	04 (67%)	04 (100%)
Gentamicin	09 (64%)	09 (64%)	11 (85%)	05 (83%)	05 (83%)	03 (75%)
Imipenem	13 (93%)	13 (93%)	04 (31%)	05 (83%)	05 (83%)	04 (100%)
Nitrofurantoin	08 (57%)	09 (64%)	09 (69%)	02 (33%)	04 (67%)	03 (75%)

DISCUSSION

Benign prostatic hyperplasia leads to urinary retention in most of the cases and emergency treatment for the retention is catheterization. Prolonged catheterization leads to urinary tract infection, bacteriuria, prostatitis, urethritis, cystitis, etc. Longer duration of catheterization leads to higher rate of infection. Robert L. et al, found that, the incidence of prostatic infection is more in prolonged catheterization (for more than 20 days) (61%) than in non-catheterized patients i.e. (38%).[10]

This study indicates that prolong indwelling catheter has two times more infection rate as compared to non-catheterized patients, which is also indicated by Mohanty (1996), who stated that pre existing urinary tract infection is not related to rate of isolation of bacteria in prostate.[11] This study coincides with our study in which, in non catheterized patients the bacteria isolated from the prostate were 38% and the bacteria isolated from the urine sample were 27% as well as in catheterized patients in which the bacteria isolated from the prostatic tissue were 61% and the bacteria isolated from the urine sample were 73%.

Mohanty and Holly (1996)[11] in their study they also observed significant incidence (42%) of bacterial growth in the prostatic tissue in patients with BPH. They obtained the sample of prostate from the patients undergoing TURP and the bacteria isolated were mostly E.coli, Coagulase negative Staphylococci and Streptococcus faecalis which is also similar to this study.

Morris and associates [12] found positive prostatic chips in 64% of patients, this study coincides with our study of total positive culture in catherized and non-catheterized patients, which is 68%.

In another study Nielson and associates (1981)[13], observed 76%of the prostatic chips had bacterial growth which is slightly higher than 68%positive culture were reported.

Drach [14] studied urine and prostatic fluid according to Meares and Stamey procedure, in addition prostatic tissue biopsies were also taken. The cultures showed that Gram positive organisms are definitely the predominant organism recovered from prostatic secretions and prostatic tissues. Since Gram positive bacteria are isolated from inflamed tissue, it can be surmised that they create prostatitis or prostatic urethritis and it seems advisable to treat gram positive prostatitis which create a significant personal problem for the patient. Gram positive prostatitis seems to be a benign disease, yet severe complications such as septicemia may occur. Most gram positive organisms from prostatitis do not grow in normal urine therefore urine culture alone should not be the criteria to analyze the presence of prostatic infection in a patient.[15]

Various other studies revealed that the common causative organisms in uncomplicated UTI are E. coli (34.4% to 67.0%), followed by Enterococcus, Pseudomonas, Enterobacter, Klebsiella, and Staphylococcus.[16-20]

Munir et al reported that E. coli was the most common organism causing bacteriuria in catheterized patients and that there was a significant association between periurethral colonization and subsequent bacteriuria.[21]

CONCLUSION

The study shows 40% of urine and 60% prostatic specimens had a positive growth in cultures. Most common organism found in urine and prostate of catheterized patients was E.coli followed by coagulase negative staphylococci and streptococcus fecalis. Whereas in the non-catheterized patients the common organisms isolated from urine were streptococcus fecalis coaglase negative staphylococci, E.coli and Enterobacter. The prostatic tissue from non catheterized patients showed similar organisms but with a high frequency.

Therefore it is suggested that sterile urine should not be taken as a definitive indicator of a sterile prostatic parenchyma .

To conclude the prostatic tissue culture along with histopathology is recommended as an aid in the diagnosis and therapy of the patient undergoing TURP as prostatic infection require an antibiotic coverage of 4-16 weeks, a culture and sensitivity test seems mandatory.

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Address for Corresponding Author:
Dr. Rizwana Barakzai
Assistant Professor of Microbiology,
Department of Pathology Sindh Medical College
Dow University of Health Sciences, Karachi.
Email: drrizwanabarakzai@hotmail.com
agha1956@gmail.com

Original Article

Complication and Causes of Hemolytic Anemia in Balochistan

1. Esaa KhanTareen 2. Haroon 3. Atif 4. Wasim Baig

1. Asstt. Prof. of Medicine, BMC, Quetta 2. PGR / MO of Medicine, BMC, Quetta 3. PGR / MO of Medicine, BMC, Quetta 4. Chief Pharmacist, Sandman Hospital, Quetta.

ABSTRACT

Objective: The aim of this study is to review the topic and to pick up cases of hemolytic anemia and to analyze their causes and complications.

Study Design: Observational and Investigative study.

Place and Duration of Study: This Study was conducted in the Dept. of Medicine, of Bolan Medical College, Quetta from March 2010 to June 2011.

Materials and Methods: 45 patients are included in our study .Their age ranged between 10 to 57 years with a mean age of 25 years. 33 were males and 12 females. About 62% of the patients turned out to have congenital hemoglobinopathies. Malaria was the predominant cause of hemolysis in acquired disease.

After initial evaluation by history and physical examination, the following diagnostic approaches were used. Evidence of hemolysis (Bilirubin, heptoglobin, hemoglobinuria), evidence of erythropoiesis (reticulocytosis,nucleated RBCs).The main causes of hemolysis were stress on peripheral film and RBC morphology. RBC morphology was the main test to suggest the further types of laboratory evaluation.

Results: About 42.2% cases turned out to have hemolysis due to congenital hemoglobinopathies. While pure beta thalassemia was seen in 20% and pure sickle cell disease in 6.6%, a combination of sickle/beta thalassemia was seen in 8.9%.In 4.4% sickle disease occurred in combination with HBc disease and 2.2% with HBD disease.G-6PD deficiency was seen in 17.8%.

Conclusion: Hemoglobinopathies contribute maximally as the cause of hemolytic anemia. HBs/Beta thalassemia, HBS/HBC from a significant percentage of congenital hemoglobinopathies.

Key Words: Hemolytic Anemia, Malaria

INTRODUCTION

Anemia is one of the most common health problem in world and Haemolytic anemia is form of anemia we often come across in our daily practice. A study was conducted to map at various causes of Haemolytic anemia in Balochistan and important causes were found to be hereditary spherocytosis, G-6PD deficiency. Autoimmune haemolytic anemia, Drugs and SLE. our main objective was not only to look into various causes of Haemolytis anemia in LOCAL population but to help physicians to be familiar with such diseases so that they not only manage them in better way but also open new door for them for future research.

MATERIALS AND METHODS

All the patients with anemia, hepatosplenomegaly, jaundice with or without fever were screened by the standard laboratory investigations all except hemolytic anemia were excluded from the study. After initial evaluation by history and physical examination, the following diagnostic approaches were used. Evidence of hemolysis (Bilirubin, heptoglobin, hemoglobinuria), evidence of erythropoiesis (reticulocytosis,nucleated RBCs).The main causes of hemolysis were stress on peripheral film and RBC morphology. RBC morphology was the main test to suggest the further types of laboratory evaluation.

i) Normal: Enzyme analysis (G-6PD status, blood film for malarial parasite, coomb's test, PNH screening.

ii) Microcytic, Hypochromic: Serum ferritin, TIBC, Hb electrophoresis.

iii) Sickle Cells: Sodium metabisulphite test, Hb electrophoresis.

iv) Spherocytes: Osmotic fragility test, comb's test.

v) Target Cells: Serum ferritin, TIBC,Liver function test,Hb electrophoresis.

vi) Schistocytes: Coagulation profile.

Other tests like liver function test, renal function test, ultra sound abdomin,immunologic assays,ECG,chest X-ray,X-ray s(spine, skill, hand),urine analysis, bone marrow examination, ,sigmoidoscopy /colonoscopy, echocardiography ,biopsy,L.D.H/heptoglobin,FDP/fibrinogen not done in all patients.

RESULTS

A total number of 45 cases were included in this study. They were admitted in Medical Unit IV of Sandeman Hospital Quetta from March 2010 to June 2011. Table 1. shows the age distribution of patients having hemolytic anemias, ranging from 10-57 years with a mean age of 25 years. Table 2 shows male and female

Table No.1: Age distribution with percentage.

Age in years	Total numbers	%age
10-20	15	33.3
20-30	22	48.9
30-40	07	15.6
>40	01	2.2
Mean Age Of 25 Years		

Table No.2: Sex distribution with percentage.

Sex Incidence	Total Number	%age
Males	33	73.3
Females	12	26.7

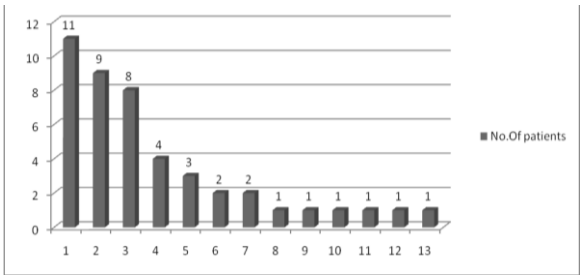

Figure No.1: frequency of various Haemolytic Anemia.

Table No.3: Percentage of 45 Patients with different Haemolytic Diseases.

Nature of Haemolytic Disease	Numbers of Patients	% age
1.Malaria	11	24.4
2.Beta Thalassaemia	09	20.0
3.G-6PD Deficiency	08	17.8
4.Sickle/ Beta Thalassaemia	04	8.9
5.Sickle/HBC	03	6.6
6.Sickle cell Disease	02	4.4
7.Comb's Negative Heamolytic Anemia	02	4.4
8.Sickle/HBD	01	2.2
9.Hereditory Spherocytosis	01	2.2
10.Hodgkin Lymphoma	01	2.2
11.Non Hodgkin Lymphoma	01	2.2
12.SLE	01	2.2
13.Snake Bite	01	2.2

ratio. Table 3 shows the frequency of various types of hemolytic anemia seen in this study. This is further illustrated by the figure 1. Hereditory hemolytic a disorder constitutes the major causes (62.2%) of hemolytic disorders. About 42.2% cases turned out to have hemolysis due to congenital hemoglobinopathies. While pure beta thalassemia was seen in 20% and pure sickle cell disease in 6.6%, a combination of sickle/beta thalassemia was seen in 8.9%.In 4.4% sickle disease occurred in combination with HBc disease and 2.2% with HBD disease.G-6PD deficiency was seen in 17.8%.Among the congenital causes hemolysis due to defect in RBC morphology (spherocytosis) was seen in one patient (2.2%). Malaria (24.4%) was the predominant cause of hemolysis in acquired disease. Lymphoma, Hodgekin's and SLE were about 7%.One patient (2.2%) admitted with history of snake bite.

DISCUSSION

Different diseases like Malaria, Thalesmia, Spherocytosis, G-6PD deficiency. Autoimmune haemolytic anemia, Drugs, SLE and its complications can cause the hemolytic anemia. In our study 45 patients were taken of different diseases.

Malaria

Their ages ranged between 12-40 years with a mean age of 27 years. Two were females with a male/ female ratio of 5.5:1.Five were coal mines labourers. All patients presented with fever ranging from five to twenty five days, three with altered consciousness. They were examined clinically and their complete blood count, Hb, reticulocyte count, liver function test including serum proteins and prothrombin time, renal function tests and electrolytes were done. Blood was also examined for malarial parasites both by thick and thin smears. Eight patients were given intravenous quinine, three with chloroquine. Five patients need blood transfusion.

Thalessmia

The diagnosis was based on clinical and laboratory investigations before the first blood transfusion. Diagnostic tests was taken before blood transfusion were given (hemoglobin level, reticulocyte percentage, MCV and MCH, peripheral blood smear, hemoglobin electrophoresis).A detailed history was taken especially family history. History of repeated blood transfusion and attacks of jaundice in the past. The ages of the patients were between 10-24 years with mean age of 18 years. Three patients were females with a male/female ratio 3:1.Fresh blood was taken on the first visit and blood smear were prepared for cell morphology examination, heamatological parameters were estimated and red cell indices were calculated. Heamoglobin electrophoresis was carried out both in alkaline and acid PH of 8.6 and 6.8 respectively. Follow up was made by clinically examination, Hb level, liver function tests, chest X-ray, ECG, Echocardiography and serum ferritin. all were advised to avoid iron supplements.

G-6PD Deficiency

The age ranged between 12-17 years with a mean age of 25 years. Three of the patients had similar episodes in the past. Two patients were developed jaundice after ingestion of Favabeans with similar attacks in the past. Four gave the history of intake of Metronidazole, Quinine and chloroquine.Of the two patients with the history of favabean ingestion, one patient was female. In all patients, peripheral smear for malarial parasite, liver function test and G-6PD status was performed.

HBSS and Sickle / Thalassaemia, Sickle / HBC Disease

Patients with sickle cell and sickle/hemoglobinopathies, five were males and five were females with a male/female ratio of 1:1.Their age ranged between 10-40 years with a mean age of 19 years. Patients were diagnosed by history, clinical and laboratory investigations including slide cover slip, sodium metabisulphate test and hemoglobin electrophoresis. Fundoscopy was done in all cases and ultrasound abdomen for gall stones. Six patients were presented with chronic pallor and splenomegaly, four patients with pain crisis and one with jaundice had the history of repeated attacks of jaundice, and one had psychiatric symptoms. patients with anemia were transfused and those with pain crisis were treated with NSAIDS and two of them needed pentazocine injections. All were well hydrated and advised to avoid dehydration and iron supplements.

Coomb's Negative Heamolytic Anemia

Two patients presented with chronic anemia, jaundice and moderate splenomegaly.Heamoglobin level, peripheral smear, reticulocyte count, G-6PD status,ANA ,anti DNA,coomb's test and Hb electrophoresis were done.

Heriditory Spherocytosis

One male patient aged 18 years presented with chronic pallor and splenomegaly of 5cm below costal margin. His blood was taken for complete blood count, peripheral smear which showed spherocytes. Patient underwent splenectomy and was advised to take penicillin V 250mg twice daily for two years.

Lymphoma

Two patients, one male aged 57 years was diagnosed to have Hodgkin's disease by lymph node and bone marrow biopsy, other male aged 16 years presented with hepatosplenomegaly and pallor was diagnosed to have non Hodgkin's lymphoma. Comb's test was performed in both and was treated with standard chemotherapeutic agents and steroids but both expired.

S.L.E

A female patient, 26 years of age, presented with the history of fever, pallor and arthralgia for a period of two months. She was diagnosed by complete blood count, immunoassay and coomb's test. She was treated with prednisolone 1mg/kg/day, then pulse therapy and blood transfusion.

Snake Bite

One patient male aged 23 years presented with the history of snake bite on his right foot. He came to hospital within six hours.His complete blood count, prothrombin time, partial thromboplastin time, FDP, urine analysis was done. He was treated with anti-tetanus, antibiotics and antivenins and the patient improved.

CONCLUSION

Hemoglobinopathies contribute maximally as the cause of hemolytic anemia. HBs/Beta thalassemia, HBS/HBC from a significant percentage of congenital hemoglobinopathies.

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Address for Corresponding Author:
Dr. Esaa KhanTareen
Asstt. Prof. of Medicine, BMC, Quetta.
E.Mail: dr.essakhan @yahoo.com
Cell No.0333-7816475

Case Report

Fibrodysplasia Ossificans Progressiva: A rare and severely disabling disease-Case Report and Review of Literature

1. Abdul Sattar 2. Azhar Mehmood Javed 3. Samreen Mushtaq 4. Maria Zahoor 5.Sadia Anjum

1. Asstt. Prof. of Radiology, NMC, Multan 2. Asstt. Prof. of Radiology, ICH, Multan 3. Radiologist, ICH, Multan 4. MO of Radiology, ICH, Multan 5. PG Registrar of Radiology, NMC, Multan.

ABSTRACT

Fibrodysplasia ossaficans progressiva is an extremely rare and severely disabling, autosomal dominant condition that effects 1 in 2 million people. We report a 3 years old female child referred to radiology department from pediatric orthopedic clinic with complaints of multiple painful swellings over the back and inability to sleep due to discomfort. Radiological investigations that include - X-Rays and C.T Scan were done that revealed heterotopic ossifications in muscles, facia and in ligaments.X-Rays revealed bilateral hallus valgus deformity with microdactyly that is characteristic of fibrodysplasia ossificans progressive.

Key words: Fibrodysplasia Ossificans Progressiva (FOP), Heterotopic Ossification, Hallus valgus deformity, 3D CT scan and Multiplanar reconstruction (MPR)

INTRODUCTION

Fibrodysplasia Ossificans Progressiva (FOP), is an extremely rare and severely disabling, autosomal dominant disease characterized by recurrent painful episodes of soft tissue swellings that lead to heterotopic ossification that is true bone formation in muscles, ligaments, fascia, tendons and joint capsules. A variety of congenital skeletal malformations of hand and feet, especially a hallus valgus deformity with microdactyly have been described as characteristic feature. [1, 3]

Incidence is 1 case per 1.64 million in United Kingdom. [4] Fewer than 600 cases have been reported in literature worldwide. [7]The condition is more common in whites, but has been reported in blacks. Females are affected more frequently than males. [2]

Pathogenesis involves over expression of bone morphogenetic protein 4 (BMP-4), which maps to 14q22-q23 [4]

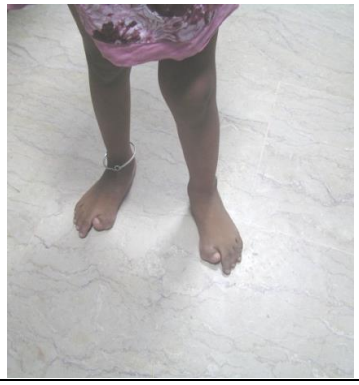
Disease process starts in early infancy, though skeletal deformities are present at birth. There is characteristic anatomical progression of heterotopic bone formation. Progressive involvement of joints leads to ankylosis. Involvement of spine causes pain and stiffness. Severe restrictive pulmonary disease may result due to involvement of muscles of chest wall. [5, 6]

CASE REPORT

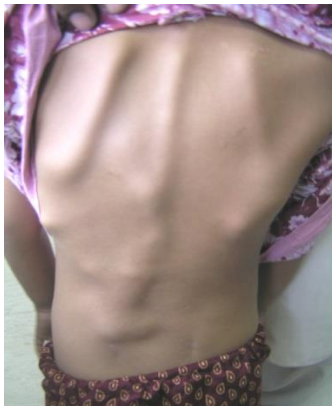
A 3 year old female child was referred to radiology department from pediatric orthopedic clinic with complaints of multiple painful swellings on the back and was unable to sleep properly due to pain.

Physical examination revealed multiple painful and hard tender swellings in paraspinal regions and along chest wall with bilateral hallus valgus deformity.

Biochemical results of mineral metabolism were with in normal limits.



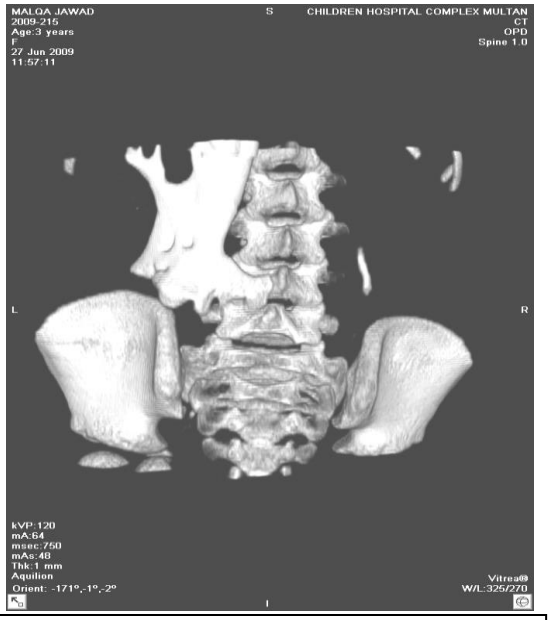
Bilateral hallus valgus deformity



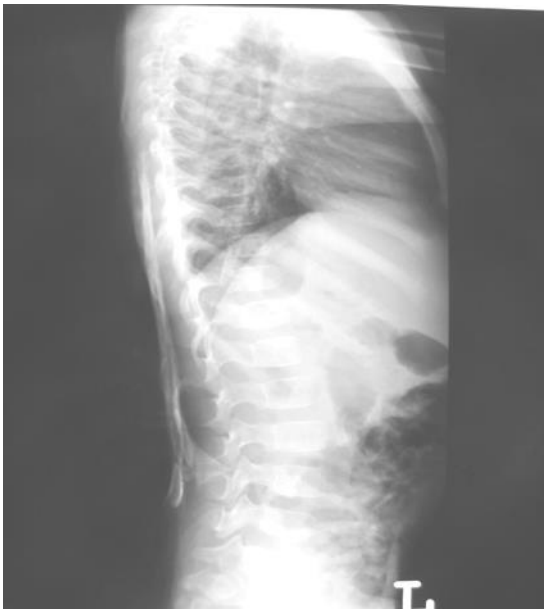
Multiple swellings on back

Digital X-rays showed heterotopic ossification along para spinal areas and chest wall with bilateral hallus valgus deformity.

CT scan spine with multiplanner and 3D reconstruction confirmed the ossification in subcutaneous location along para spinal regions and chest wall.



3 D CT scan showing heterotopic bone formation on back.



X-Ray spine showing heterotopic ossifications in paraspinal area

Patient was send back to the orthopedic surgeon with the diagnosis of FOP

DISCUSSION

FOP, though extremely rare, is by no means new, with reports in the scientific literature as early as 1692.There is no effective treatment for the heterotopic ossifications of FOP[2, 3]. Thus successful management relies on early recognition of this disorder and prevention of inciting inflammation or injury. Especially important is the avoidance of precipitating factors such as biopsies, intramuscular injection, prolonged pressure on body, aggressive physical therapy, falls etc.Soft tissue ossification occurs in response to inflammation or trauma and the pattern of heterotopic ossification that results, is unique to each patient[5]. Frequent sites of heterotopic ossification are paraspinal regions especially in thoracic and the shoulder girdle. Most patients are misdiagnosed despite the presence of pathognomonic changes of the first toe, even evident clinically at birth. [1],[3]

The combination of hallus valgus deformity of first toe and posterior thoracic soft tissue masses are highly suggestive of FOP.A mis-diagnosis rate of 87% has been reported. Soft tissue swelling and heterotopic bone was wrongly attributed to neoplasm in 32% of patients, and 67% of patients had unnecessary biopsies [4]

With awareness of characteristic radiological findings, the radiologist might be the first to recognize the constellation of findings, suggest the correct diagnosis and prevent iatrogenic injury in this rare disorder. No biopsy was done in our patient

CONCLUSION

Although FOP is a rare disease, however awareness of characteristic physical & radiological findings should able the radiologist and pediatrician to make early diagnosis that can avoid unnecessary iatrogenic injuries and flaring up of the disease process

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Address for Corresponding Author:
Abdul Sattar,
Radiology Department,
Nishtar Medical College & Hospital,
Multan, Pakistan
+92-333-4354512
E-mail. drasanjum@gmail.com