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Editorial

Asthma: On the Rise

MohsinMasud Jan
Editor

The death rate from asthma attacks is steadily creeping up. Asthma is a common chronic inflammatory disease of the airways characterized by reversible airflow obstruction, and bronchospasm. Symptoms include wheezing, coughing, chest tightness, and shortness of breath. The diagnosis is made clinically.[1] These symptoms vary over time, and from individual to individual.

More than 300 million people worldwide suffer from this disabling disease and this figure is projected to rise by nearly 50% every decade.[2] The International Study of Asthma and Allergies in Childhood (ISAAC) study mentioned a prevalence of 8% in Pakistani paediatric population back in 2008.[3] The current prevalence is estimated to be around 11%, though the figure has not been confirmed.

The first sign of disease is a persistent cough. Symptoms may occur several times in a day or week in the effected. For some people the symptoms become worse during physical activity or at night. Failing to recognize triggers that lead to a tightened airway can easily be fatal.

The major risk factors for developing asthma are:familial atopic background, urban residence, passive smoking and early weaning were important risk factors for childhood asthma,[4] exposure to indoor allergens such as house dust mites in bedding, carpets, curtains, stuffed furniture; pollution, exposure to cats and dogs in the first two years of life, cockroaches; and outdoor allergens such as pollens, moulds; tobacco smoke and chemical irritants. Other minor risk factors includeprenatal exposure to active maternal smoking, exposure to second hand smoke after birth, respiratory infections in childhood, low birth weight, obesity, persistent allergic rhinitis, scented cosmetics, and medicines such as aspirin and beta-blockers. Asthma triggers include cold air, extreme emotional arousal and physical exercise.

The most alarming factor; there is no cure for asthma, even though there are some very effective medicines which, when properly used, can largely control asthma attacks and allow people to lead a normal life.Correctly using anti-asthma medication and avoiding allergens is really the cornerstone in achieving control. Inhalers are the first line of treatment and are the safest way of delivering medicine to the lungs. Preventive measures include;reduction in level of exposure to common risk factors including smoking and environmental tobacco smoke, indoor air pollutants and keeping indoor humidity low, maintaining a healthy weight, controlling insects such as cockroaches, and not keeping pets inside the house.

Every year the Global Initiative For Asthma holds aWorld Asthma Day. In 2015, it took place on Tuesday, May 5, 2015 and the theme was "You Can Control Your Asthma." GINA also continued to use the sub-theme, "It's Time to Control Asthma." Planning seminars for public awareness, and observing the World Asthma Day, could serve as important milestones in increasing awareness in the public and us doctors alike.

It is time that we, the doctors of this country try to realize the gravity of this situation. If statistics are to be relied upon, nearly every 11th child in our country could be asthmatic, and we need to strive towards improving care and diagnosing asthma properly and in a timely fashion in our paediatric population.

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Original Article

Tuberculous Lymphadenitis

Presentation and Aetiological Aspects of Tuberculous Lymphadenitis at District Sialkot

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1. Senior Consultant Surgeon, 2. WMO/Registrar 3. House Officer, Dept. of Surgery, S.A.R Gardezi Ward, Khawaja Muhammad Safdar Medical College, Sialkot

ABSTRACT

Objective: The present study was conducted to assess the presentation and etiological aspects of tuberculosis cervical lymphadenopathy for early detection, diagnosis and prompt specific therapy.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Department of Surgery and ENT of Allama Iqbal Memorial Hospital Sialkot from July 2009 to July 2014.

Materials and Methods: Data was collected including history, family history, socioeconomic status, history of contact and symptoms. They have already undergone FNAC and only those with inconclusive FNAC underwent excision biopsy.

Results: Total sample size was 372 males and females were 232, age range of 6 to 70 years. The younger was a newborn of 2 months of age with history of tuberculosis in mother and the oldest was a 70 year of age with prolonged history of pulmonary tuberculosis.

Conclusion: Frequency of tuberculosis is more common in Sialkot district. The main reason of prevalence of tuberculosis is poor hygiene, poverty, overcrowding, tanneries spill over contaminating drinking water. Timely diagnosis is better option in order to reduce such incidence and therapy reducing cost of treatment.

Key Words: Mycobacterial infection, Tuberculosis, FNAC, Excision biopsy, Migrant

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INTRODUCTION

Tuberculosis is one of the commonest cause of peripheral lymphadenopathy in most countries of Asia and Africa with varying frequency of 4-56%.[1] It has become one of the major health problem in population with an estimated one third of world population and 3-4 million new cases are found every year. [2] The body has approximately 600 lymph nodes, Only those in Submandibular, Axillary or Inguinal regions may normally be palpable in healthy people.[3]

Chronic cervical lymphadenopathy (Enlarged lymph nodes for more than 3 weeks) may result from a variety of different underlying diseases.[4] Cervical lymphadenopathy is usually defined as cervical lymph nodal tissue measuring more than 1 cm in diameter.[5] In the world various etiological reasons are described for this increasingly becoming problem.[6] One of the commonest extra pulmonary manifestations of Mycobacterial infection is cervical tuberculosis lymphadenopathy especially in the developing countries.[7] Painful tuberculosis lymphadenitis previously termed Scrofula, is a unique manifestation of disease due to organisms of Mycobacteria Tuberculosis complex.[8] Tuberculosisly mphadenitis usually present as a slowly progressive painless swelling of a single group of lymph node.[9] The duration of symptoms at time of presentation is typically 1-2 months, varying from 3 weeks to 8 months.[10]

The mean duration of symptoms were significantly longer in men than in women.[11] Cervical lymphadenopathy may be unilateral, bilateral, isolated, matted and variable in their consistency from firm or solid in nature.[12,13] It can occur in all age groups and nearly any organ can be involved. Sialkot being an industrial city due to leather industries, poverty, illiteracy, lack of social awareness and poor hygiene conditions are highly susceptible to tuberculosis. The problem has further been aggravated by lack of health facilities to them, lack of proper diagnostic and therapeutic problem in primary care. Patient referral to special unit with delay and referral for unneeded diagnostic and therapeutic procedures, misuse of trial antibiotics may lead to Tuberculosis.

The present study was conducted to assess the presentation and etiological aspects of tuberculosis cervical lymphadenopathy for early detection, diagnosis and prompt specific therapy which can result in better control and prevention, a rationale for conducting such study was to deliver knowledge to community health workers regarding its prevalence and early diagnosis;

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hoping to contribute to the making of a better and more affective system for diagnosing these patients.

MATERIALS AND METHODS

This Descriptive study was conducted in the busiest surgical unit of Allama Iqbal Memorial Teaching Hospital, Sialkot from July 2009 to July 2014. Data was collected which included (Diameter, texture and tenderness), others(Sex, history including family history, family background, socioeconomic status & history of contact), Duration, Associated signs & symptoms and Location.

Different modalities of investigations are used which include the FNAC, Automatic core needle biopsy, flow cytometry, radiological guided core needle biopsy and open biopsy. Fine needle aspiration was performed in all patients and open biopsy with FNAC results were inconclusive or with abnormal findings (abnormal white blood cells, WBC's abnormal blood film, high ESR > 20 ml/hr, PPD > 10 mm)

RESULTS

Table No.1: Age Distribution

Sr. No.	Age (Years)	Male	Female	Total
1.	0-10	14	7	**21**
2.	11-20	140	113	**253**
3.	21-30	94	54	**148**
4.	31-40	36	27	**63**
5.	41-50	18	14	**32**
6.	51-60	14	11	**25**
7.	61-70	9	6	**15**
Total		**327 (58.5%)**	**232 (41.5%)**	**559**

Table No.2: Presenting Symptoms

Sr. No.	Symptoms	No. of Patients	% age (out of total)
1.	Neck swelling	557	99.6
2.	Fever	407	72.9
3.	Pain	397	71.0
4.	Cough	271	48.4
5.	Weight loss	225	40.2
6.	Generalized weakness	361	64.5

Table No.3: Site of Disease

Anterior Triangle	Posterior Triangle
295	264

Table No.4: Lymph Nodes Involved

Multiple	Single
443	116

Table No.5: Site of Lymph Nodes Involved

Only Cervical	Cervical & Associated Regions
470	89

Table No.6: Side of Lymph Node Involved

Unilateral	Bilateral
344	215

Table No.7: Demographic Distribution of Patients

S. No.	Demographic Area	Total (%)
1.	URBAN	220 (39.3)
2.	RURAL	289 (51.6)
3.	MIGRANTS OF SWAT	50 (8.9)

Table No.8: Socioeconomic Status

S. No.	Socioeconomic Status	Total (%)
1.	Lower	349 (62.4)
2.	Middle	190 (33.9)
3.	Upper	20 (3.5)

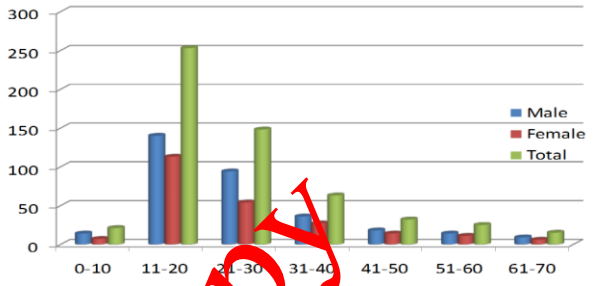

Figure No.1: Age Distribution

DISCUSSION

Tuberculosis is becoming of the major health problems and one of the infectious diseases which involves lymphatic system of body.[7] Its spread in most countries of Asia and Africa cannot be ignored. Pakistan is also a victim of this disease. In our study, males (58.5%) dominated the females (41.5%). Males were predominantly involved with Tuberculosis in this study while more females were reported in a study from India.[14] The Median age of the patients was 21.5 years, mostly presented between the 1st and 2nd decade of life, which is not in accordance with other local studies.[15,12] However its involvement of lower socioeconomic status which is also agreed by the studies conducted by Jidal N[16] and local authorities.

As this disease is a disease of poor people, the data suggests that most of the patients belonged to rural were of poor socioeconomic conditions, poor ventilated, overcrowding and unhygienic conditions. Family history of contact was usually denied as a social stigma but when asked indirectly like cause of death of their elders and history of cough and other constitutional symptoms initially denied later accepted and denial was regretted. Constitutional symptoms were present in very few, mostly will present with neck swelling.

Demographic distribution of patients 289 was Rural, 220 Urban and 50 Immigrants came from Swat, Gilgit and Waziristan which is not in accordance with the study carried out at PGMI Lady Reading Hospital Peshawar on 100 cases. [17]

Mobility, Softness and tenderness are almost always associated with reactive changes which is similar to observations made by other investigator.[18]

In our study the result showed that most common presentation was neck swelling which was present in 99.6 % of cases, other presenting signs and symptoms were generalized weakness, weight loss, fever & headache as shown in table. In a similar study it was found that 100 % of patients presented with painless neck mass, followed by fever 63.7 % and weight loss in 41 % of patients.[19]

There was not marked difference of involvement of anterior triangle and posterior triangle, 70 % have both anterior and posterior triangle involved which is not in accordance with other studies conducted by K AV et al* showed the posterior cervical lymph nodes were the commonest and affected in 40 % of cases.[20]

Size of lymph nodes measured with a ruler or a vernier caliper and their length and width noted in mm or cm. Enlarged lymph node were less than 3 cm or equal to 3 cm in 369 cases while in 190 cases it was more than 3 cm. Consistency of lymph nodes was viewed. It was solid in 300 cases while 162 cases it was cystic, 97 cases swelling with sinus formation.

The Tuberculosis was diagnosed firstly by FNAC in most of cases while open biopsy was carried out in those cases where FNAC was inconclusive. These results are largely variable to Maharjan M, et al where FNAC was found to be effective diagnostic method (94%). FNAC is a reliable diagnostic tool in a case of tuberculosis cervical lymphadenopathy but surgical excision has been recommended for Paradoxical Upgrade Reaction (PUR) for treatment purposes in cases of tuberculosis lymphadenitis and for patients who have discomfort from tense fluctuant lymph nodes.

CONCLUSION

Frequency of Tuberculosis in cervical lymph nodes is more common in Sialkot District. The main reasons for high prevalence of Tuberculosis are poor hygiene, poverty, and overcrowding and tanneries spill over contaminating drinking water. Timely diagnosis is critical in lowering such incidence and therapy reducing overall health care cost.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Role of Ca. Blockers in Diabetes

Cardiovascular and Renal Protection in Type 2 Diabetic Hypertensive Patients. The Role of Calcium Channel Blockers

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ABSTRACT

Objective: To study the effects of Calcium Channel Blocker (Amlodipine) as monotherapy in diagnosed hypertensive, non-insulin dependent diabetes mellitus (NIDDM) patients.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at Jinnah post graduate medical centre (JPMC) Karachi, in collaboration with the department of medicine JPMC, Karachi from July 2010 to January 2011.

Materials and Methods: This study is to examine the effects of Amlodipine in type 2 diabetic hypertensive patients with base line proteinuria. 20 normal subjects were also selected as a control group.

Results: with CCB (Amlodipine) baseline to final change for SBP as well as DBP was significantly reduced i.e. 24.70 % ($p<0.001$) and 16.20% ($p<0.001$) respectively. CCB showed 44% ($p<0.001$) reduction in FBS, creatinine clearance reduced by 8.10% ($p<0.5$), serum potassium reduced by 4.50%, non significant increase in serum urea i.e. 3.70% and serum creatinine i.e. 3.8% was observed.

Conclusion: Aim of treating hypertension is to control or limit its cardiovascular complications; CCBs are the drug of choice in controlling blood pressure and to prevent the progress of cardiovascular events in patients without diabetic nephropathy as well as reserves for add-on therapy in hypertensive patients complicated with diabetic nephropathy.

Key Words: Cardiovascular, Renal Protection, Diabetes Hypertension, Calcium Channel Blockers

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INTRODUCTION

In an estimate by world health organization currently 170 million people are affected by diabetes mellitus that will grow up to 370 million by the year 2030. Renal function is declining in half of these affected patients[1]. Most commonly occurring comorbid conditions are hypertension and diabetes mellitus. The prognosis of a combination of diabetes and hypertension is particularly very poor[2]. It is recommended in the 7th report of Joint National Committee and European society of hypertension guideline that patients having systolic blood pressure more than 20 mmHg and diastolic 10 mmHg above the treatment goals should be considered for treatment with combination therapy. It is also advised for patients with cardiovascular and other risk factors[3,4]. The most promising combination that is highly effective and easily tolerated by the patients is calcium channel blocker and angiotensin receptor blockers.

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Morbidity and death related to hypertension can be reduced to a large extent with antihypertensive therapy. For the prevention of cardiovascular diseases in high risk individuals and to control blood pressure amlodipine is the most suitable agent from the class of calcium channel blockers. It is documented that angiotensin converting enzyme inhibitors and CCBs are helpful in reducing cardiovascular complications in hypertensive patients; however, the best choice to start therapy is still uncertain[5]. Amlodipine can control blood pressure in young adults and elderly patients that is proven in many research trials[6]. It also provides vasculoprotection independent of its blood pressure lowering effect[7]. Calcium channel blockers are more suitable agents to treat hypertension in patients of kidney transplant due to their vasodilation property at preglomerular level[8].

It is also established in previous studies that glucose tolerance and low levels of insulin are improved with amlodipine[9]. CCBs improve insulin sensitivity and secretion in tissues sensitive to insulin by causing

vasodilation without activating sympathetic nervous system [10, 11]. Metabolic effects of amlodipine are exerted by its antioxidant effects. Inhibition of glucose transporters and glycogen synthase by calcium is also prevented by calcium channel blockers[12, 13]. Multiple hemodynamic beneficial effects of CCBs make them valuable to treat high blood pressure and related cardiovascular disorders.[13]

MATERIALS AND METHODS

The study was conducted in Jinnah post graduate medical centre (JPMC) Karachi, in collaboration with the department of medicine JPMC, Karachi from July 2010 to January 2011.

Minimum forty patients with NIDDM were selected from medical OPD and diabetic clinics of JPMC, Karachi. All had mild to moderate hypertension which was not previously been treated and were suitable for first line antihypertensive therapy. 20 normal control subjects apparently healthy and not taking medication were included after excluding an0y medical illness.

Inclusion criteria were defined as follows, newly diagnosed and untreated patients with mild to moderate hypertension between 30-65 years of ages, duration of diabetes more than 10 years with FBS > 140mg/dl and persistent proteinuria. Patients with history of malignant hypertension, myocardial infarction, coronary artery bypass surgery, unstable angina, cardiac failure, insulin dependent diabetes(IDDM) with renal failure or impaired hepatic function, pregnancy or having allergy to the medications involved in the study were excluded from the study. Two patients dropped out from the study while the remaining completed the study successfully.

All patients underwent an initial 12 weeks' dietary titration period before starting antihypertensive therapy (controlled period). They were then assigned to receive the study medication i.e. tablet Amlodipine 10 mg once a day for a period of 12 weeks. Blood sugar level was controlled by Glibenclamide 5 mg, the dose of which was adjusted according to the glycemic control. 24 hour urinary proteins, serum urea, serum creatinine, serum potassium and creatinine clearance were measured 6 weekly while systolic and diastolic blood pressure and FBS was measured fortnightly. Throughout the study period the patients were advised to take a diabetic diet. Blood pressure was measured in sitting position in the morning OPD every fortnight according to recommendations of the 7th JNC published in 2003 [3].

RESULTS

38 diagnosed hypertensive type 2 diabetic patients with albuminuria were studied and 20 normal subjects were also selected for the control group. No concomitant antihypertensive or diuretic therapy was given throughout the study. Table 1 shows the baseline characteristics of the patients enrolled in the study.

Table No.1: Base line characteristics of the patients

Characteristic	Amlodipine Group (N=38)	Control Group (N=20)
Age (years)	52±7	50±5
Male	24(63.15%)	12(65.5%)
Female	14(36.8%)	8(34.5%)
BMI	31±6	30±8
Urinary proteins (mg/24hrs)	329.79±261	22±5
Systolic Blood Pressure (mmHg)	151±9	113±11
Diastolic Blood Pressure (mmHg)	96±6	73±8
FBS (mg/dl)	159±53	86±15
Serum urea (mg/dl)	34±9	24±5
Serum creatinine (mg/dl)	0.87±0.13	0.86±0.13
Creatinine clearance (ml/min)	102±27	92.7±8.8
Serum potassium (mmol/l)	4±0.57	3.56±0.31

Table No.2: Changes in the various parameters from day 0 to day 90 of the treatment with tablet Amlodipine 10mg / day

Parameters	Day-0	Day-45	Day-90	Change %
Urinary proteins (mg/24hrs)	329.79±261	325.90±258	316±194	4.20 (NS)
Systolic Blood Pressure (mmHg)	151±9	120±8	113.95±7.9	24.7 (p<0.001)
Diastolic Blood Pressure (mmHg)	96±53	80±7	80±9	16.2 (p<0.001)
FBS (mg/dl)	159±53	99±12.8	89±13.8	44 (p<0.001)
S.urea (mg/dl)	34±9	34.8±4.7	35±3.8	3.70 (NS)
S.creatinine (mg/dl)	0.87±0.13	0.88±0.10	0.90±0.12	3.8 (NS)
Creatinine clearance (ml/min)	102±27	94±18.7	94±14	8.10 (p<0.05)
S.potassium (mmol/l)	4±0.57	4±0.55	4±0.52	4.50 (NS)

Table 2 shows the effects of CCB (amlodipine) monotherapy on various laboratory parameters (see figure # 1). There is significant reduction in systolic blood pressure (SBP) from baseline by 24.70% i.e. from 151mmHg to 113mmHg (p<0.001%). Diastolic blood pressure (DBP) also declined by 16.20% i.e. from 96mmHg to 80mmHg (p0.001%) on day 90th of the treatment. Creatinine clearance reduced by 8.10% i.e. from 102.3±27.3 on day 0 of the treatment to 94.03±14.6 ml/min on day 90 of the treatment. A significant reduction (44%) of fasting blood glucose was also observed on day 90th of the treatment i.e. declining from 159mg/dl to 89mg/dl (p0.001%). A

significant increase of 3.70% i.e. from 34.32±9.26 to 35.59±3.89 was observed in serum urea. Also a non significant increase was observed in serum creatinine of 3.8mg/dl during the study. Non significant decrease of 4.50% in serum potassium level was observed on completion of study.

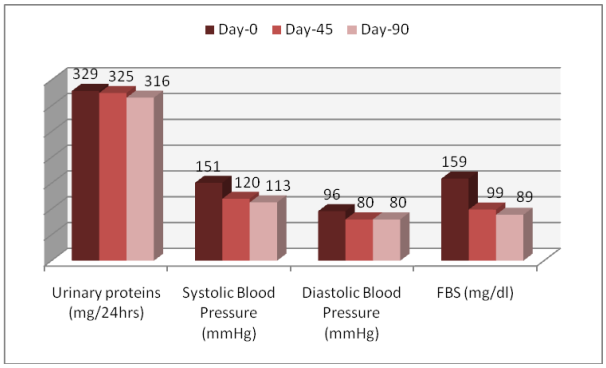

Figure No.1: Changes in various parameters from Day0, 45 & 90 of the treatment with Amlodipine

DISCUSSION

This study is the clinical trial of CCB (Amlodipine) in hypertensive diabetic patients for a period of three months. In this study 20 subjects were kept in control (group N), their mean urinary protein was 22.63± 5.28mg/24hrs, which is less than the recommended range of 300mg/24hrs.In current study, we found significant reduction in Systolic and diastolic blood pressure i.e. 24% and 16% respectively which coincides with the results found by lino that is 11% reduction in SBP and 15% reduction in DBP[15]. Several studies have reported that calcium antagonists improves target organ damages and the clinical outcome in patients with hypertension [16].Study conducted by agerloa concluded an increase in proteinuria by 58% in patients treated with amlodipine, disfavors our study showing a reduction of 4.20% in proteinuria, while other parameters are consistent with our findings[17]. Another study by kuriyama showed an increase in proteinuria by 11% and unchanged serum potassium with CCB compared with our study where a decrease of 4.2% proteinuria and 4.5% reduction in serum potassium was observed [18]. It is proven in previous studies that there is increased prevalence of insulin resistance amongst patients with essential hypertension. Standard antihypertensive agents can be used but there are particular problems in their use especially in NIDDM patients, like thiazide diuretics inhibit, the secretion of insulin and beta blockers impair insulin sensitivity, whereas CCBs (amlodipine) decreases insulin resistance[19]. Role of calcium channel blocker was also evaluated in diabetic hypertensive patients and found that amlodipine apart from decreasing blood pressure also decrease blood glucose levels[20]. In our study there is significant reduction in serum blood glucose levels i.e. 44% supported by the study conducted by Erosy this may explain a decrease in insulin resistance with amlodipine19.

At the end of the discussion we concluded that selecting specific antihypertensive therapy, is the most important decision made in the treatment process. In older days beta blockers were the drug of choice for initial therapy, but they are replaced by newer antihypertensive drugs because of their failure to protect against coronary artery disease. Long acting CCBs, particularly amlodipine, in hypertensive patients for protection of cardiovascular events are as effective as other antihypertensive agents. Amlodipine can be safely combined with other antihypertensive drugs including diuretics to provide early and effective blood pressure control in high risk patients[21]. CCBs in combination with ARBs have potentially useful antiproteinuric effect in patients with type 2 diabetic nephropathy, even when their renal function is reduced[22]. CCBs provides sustained antihypertensive activity over 24 hrs, among them amlodipine seems to be the drug of choice in controlling blood pressure and prevents the progress of cardiovascular events in patients without diabetic nephropathy because of its low side effect profile. CCBs also reserved for add-on therapy to achieve effective blood pressure control in hypertensive patients complicated with diabetic nephropathy.

CONCLUSION

Aim of treating hypertension is to control or limit its cardiovascular complications; CCBs are the drug of choice in controlling blood pressure and to prevent the progress of cardiovascular events in patients without diabetic nephropathy as well as reserves for add-on therapy in hypertensive patients complicated with diabetic nephropathy.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Effects of Interferon on Thyroid

Effects of Interferon Alpha on Thyroid Functions during Treatment of Chronic Hepatitis C

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ABSTRACT

Objective: The aim of the study was to assess the incidence, types and risk factors of thyroid dysfunction and thyroid autoimmunity, and to correlate the laboratory parameters with clinical findings.
Study Design: Prospective clinical trial
Place and Duration of Study: This study was conducted at General hospital, Lahore from March, 2011 to December 2011.
Materials and Methods: The study enrolled sixty diagnosed patients of chronic hepatitis C with normal baseline thyroid hormone levels (TSH, FT3, FT4). Anti-thyroid peroxidase antibodies (anti-TPO-Ab) were also assayed. Baseline results were compared with those obtained during and at the end of interferon-alpha (IFN- α) and ribavirin combination therapy.
Results: Incidence of thyroid dysfunction was 10%. Six patients (10%) developed thyroid dysfunction. Subclinical hypothyroidism was more common. Four female patients developed hypothyroidism and 2 patients showed hyperthyroidism. The overall incidence of anti thyroid peroxidase antibodies (anti-TPO-Ab) before treatment was 1.7% which became 5% at the end of therapy.
Conclusion: Female sex and anti-thyroid peroxidase antibodies (anti-TPO-Ab) either present before or during treatment at are at risk of developing thyroid dysfunction, so all the patients of chronic hepatitis C should be screened for thyroid functions and anti-thyroid peroxidase antibodies (anti-TPO-Ab) before treatment with interferon-alpha (IFN- α) & ribavirin combination therapy, and be monitored during and after treatment.
Key Words: Interferon Alpha. Autoimmunity. Anti-thyroid peroxidase antibodies, HCV..

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INTRODUCTION

Chronic hepatitis C is a liver disease caused by hepatitis C virus (HCV). The hepatitis C virus was recognized in 1989 and since then hepatitis C virus (HCV) has been considered as a major public health problem all over the world including Pakistan.[1] Hepatitis C virus produces liver infection in more than 180 million people worldwide[2]. In Pakistan about 10 million people have the hepatitis C virus (HCV) infection, although accurate epidemiological information for chronic hepatitis C virus (HCV) infection is still not available[3]. These patients are more prone to develop hepatocellular carcinoma due to constant infection[4]. At least 250,000 deaths per year are due to hepatitis C[5]. Factors known to increase the progress to cirrhosis include, old age at HCV acquirement, male sex, heavy alcohol intake, and co-infection with either Hepatitis B or HIV[6]. Treatment for chronic hepatitis C has become better over the last decade and it is generally recommended in patients under the age of 70 years[7]. The purpose of the treatment is to achieve an undetectable HCV-RNA six months after treatment[8]. Interferon alpha (IFN) in combination with Ribavirin has been used in the treatment and become standard treatment for Chronic Hepatitis C since French consensus conference in 2002[9]. Interferons (IFNs) were discovered and named by Isaacs and Lindenmann in 1957 who observed that virus-infected culture formed a protein that reacted with cells, making them resistant to infection by other viruses[10]. Interferon-alpha regular or pegylated in combination with ribavirin is used and this results in sustained virological response in about 80% of cases with genotype 2 and 3 CHC infection and 40-50% in genotype 1 infection.[11,12]

Adverse effects of IFN treatment include flu-like symptoms, fever, malaise, muscle aches, neuropsychiatric symptoms and endocrinal dysfunction[13, 14]. The most important endocrine gland affected is thyroid gland[13, 14]. Hypothyroidism or hyperthyroidism may occur in up to 5-20% of patients especially in those with anti-thyroid antibodies present before treatment with interferon alpha and ribavirin[15]. Interferon alpha treatment may activate the production of different types of auto-antibodies such as antinuclear

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antibodies (ANA), thyroid peroxidase antibodies (TPO) and anti thyroglobulin (TGA) antibodies[16].

Thyroid dysfunction is the most common autoimmune disorder related with Interferon alpha treatment and the occurrence of thyroid dysfunction due to interferon alpha was recognized in 1985 in patients who underwent interferon alpha treatment for carcinoid tumors and breast cancer[17]. The important factors that play role in the development of thyroid disease during Interferon alpha therapy are female gender and presence of thyroid auto-antibodies particularly anti-thyroid peroxidase antibodies(TPO-Ab) prior to treatment[18].

The common form of thyroid autoimmunity is the presence of thyroid peroxidase antibodies (TPO-Ab), and thyroglobulin antibodies (Tg-Ab). The newer immunoassays have improved sensitivity to detect thyroid peroxidase antibodies (TPO-Ab) than the older assays[19].

MATERIALS AND METHODS

60 patients of either sex were enrolled for the study. Written consent, for participation in the study, was taken from each patient.

Inclusion criteria: Diagnosed patients of Chronic Hepatitis C (CHC) with normal thyroid functions.

Exclusion criteria: Abnormal thyroid function tests before the treatment and the co-existence of other disease that need chronic drug therapy. Serum levels of TSH, FT4, FT3 and TPO-Ab were assayed using enzyme immunoassay test kits, catalog no, BC-1001, 1008,1006 Biocheck inc, 323 Vintage park. All patients were assessed clinically too. Patients were treated with interferon alpha and ribavirin by their physician. The duration of treatment was 24 weeks and all patients were tested for thyroid hormones and thyroid peroxidase auto-antibodies (TPO-Ab) at week 0, 12 and 24 of treatment with Interferon alpha and ribavirin.

Data Analysis: The data was analyzed using SPSS 16.0 (Statistical Package for Social Sciences). Mean ± S.D is given. Frequencies and percentages are given for qualitative variables. Graphs are presented for both quantitative and qualitative variables. Paired sample t-test is applied to observe pair wise differences for normally distributed quantitative variables. A p-value of <0.05 was considered as statistically significant [20].

RESULTS

Among 60 patients participated in the prospective clinical study, 26 were males with mean age 41.77±8.53 and 34 females with mean age 42.71±8.36 years. The overall mean age was 42.30±8.37 years (Table.1).

Table No.1: Distribution of cases by age and gender

	Male		Female		Total	
Age (Years)	N	%	N	%	N	%
31 – 40	15	57.7	20	58.8	35	58.3
41 – 50	8	30.8	9	26.5	17	28.3
51 – 60	3	11.5	5	14.7	8	13.3
Total	26	100.0	34	100.0	60	100.0
Mean	41.77±8.53		42.71±8.36		42.30±8.37	

After treatment with interferon alpha and ribavirin for 24 weeks, fifty four (90%) were having normal thyroid functions. Six patients (10%) developed thyroid dysfunction biochemically, four patients(6.6%) developed hypothyroidism, all were females with age ranging from 35-58 years. two patients(3.4%) developed hyperthyroidism. When the test of normality was performed by using Shapiro-Wilk test the results were deviating from the normality with p-value< 0.001. Among thyroid function tests the value for FT3 was raised by 2.013± with p-value 0.999. The value for FT4 was declined by 0.13± 0.36 pg/ml with p-value 0.006 which was insignificant statistically. Thyroid auto-antibodies (TPO-Ab) were present in 1.5% of patients before the start of treatment and in 5% after the treatment with p-value. 0.662 , which was insignificant statistically.(table 2)

Table No.2: Thyroid function tests of the patients showing thyroid dysfunction

Age (years)	Gender	TSH		FT3		FT4		TPO-Ab	
		Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
50	Female	2.4	6.8	1.151	1.139	0.94	0.41	10.6	85.47
52	Female	2.69	8.35	1.45	0.83	0.96	0.22	0.79	15.70
58	Female	2.84	10.41	1.4	0.89	0.83	0.29	5.58	125.62
57	Female	2.65	8.32	2.60	1.124	0.87	0.295	8.30	15.40
54	Female	0.42	0.99	1.43	4.36	1.87	3.37	80.59	92.50
45	Male	0.85	0.32	2.78	4.61	1.15	3.92	17.58	23.22

All the patients enrolled for study were examined clinically before starting treatment and after the completion of treatment with interferon alpha and ribavirin. Ten patients(16.7%) were having cold sensitivity with p-value<0.001.Tremors, heat intolerance and mental slowness was observed in 2, 1 and 2 patients respectively with p-value>0.005.

DISCUSSION

Treatment of Chronic Hepatitis C with Interferon alpha and ribavirin may lead to many adverse effects. Abnormal function of thyroid gland is a known side effect or complication during IFN alpha and ribavirin combination therapy. Thyroid dysfunction is more common in females, and hypothyroidism occurs more frequently, and resolves after the end of therapy. IFN interacts with specific receptors present on the cell surfaces and leads to activation of various signaling pathways via very complex sequence of interactions and activation of gene transcription.

In present study the baseline thyroid functions i.e. serum TSH, FT3 and FT4 were normal in all sixty patients participating in study. Baseline (week 0) results were compared with those obtained at weeks 12 and 24 of therapy. Biochemical thyroid dysfunction (TD) developed in 6 patients (10%) out of 60 patients. Hypothyroidism was common as compared to hyperthyroidism. The incidence of hypothyroidism was 6.6% and 4.3% of the patients in the study developed hyperthyroidism. Also all hypothyroid patients were females i.e. four patients (6.6%). Two patients developed hyperthyroidism, one male (3.3) and one female (3.3%). In most of the patients, these disorders occurred during the early course of treatment as has been reported in various studies. Interferon alpha induces a rush of immune reactions in the body.

This is related to immuno-modulatory properties of Interferon (IFN) which induces non-organ specific antibodies causing thyroid dysfunction. Recent reports suggest that Interferon alpha has direct toxic effects on thyroid gland, along with immuno-modulatory mechanisms. The level of thyroid peroxidase antibodies rose from 1.7% at baseline to 5.00% at the end of treatment,i.e.24 weeks, also these antibodies were detected in those female patients who had a higher mean age group which, is characteristic of autoimmune thyroiditis. These results suggest that female patients with Chronic Hepatitis C receiving Interferon alpha therapy are more prone to develop thyroid abnormalities. All the above findings support the view that Interferon alpha therapy in patients with Chronic Hepatitis C accentuates and makes clinically manifest pre-existing autoimmune thyroid abnormalities. We cannot exclude genetic factors to play an important role in the risk for thyroid dysfunction (TD).

In the present study the enrolled patients were assessed clinically too. It was found that all patients were free from any symptom regarding thyroid gland before starting the treatment. At the end of therapy it was found that no patient undergoing IFN alpha therapy showed overt thyroid dysfunction; only subclinical hypothyroidism and hyperthyroidism was observed.

Lastly, thyroid dysfunction caused by interferon alpha and ribavirin combination therapy is a common finding in these patients. Interferon can lead to the appearance of different manifestations of thyroid disease, ranging from subclinical hypothyroidism to overt hypothyroidism or hyperthyroidism. Female gender and the presence of anti-thyroid antibodies are important predisposing factors that may cause thyroid dysfunction . Permanent hypothyroidism is more common and this may necessitate hormone replacement therapy. Thyroid function tests should be checked before the start of treatment and periodically during the treatment and at least once in the six months following IFN alpha treatment.

CONCLUSION

Treatment with Interferon alpha in the patients of Chronic Hepatitis C is associated with thyroid dysfunction and thyroid autoimmunity. The mechanism of interferon induced thyroid dysfunction (IITD) is not very clear but it may be due to the direct toxic effect of interferon alpha on thyroid gland or may be immune mediated. long-term follow-up of patients with thyroid dysfunction due to interferon alpha thyroid is necessary to determine its relation to sustained virological response (SVR).

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Cholecystectomy

Frequency and Causes of Conversion of Laparoscopic Cholecystectomy into Open Cholecystectomy

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ABSTRACT

Objective: To determine the frequency and causes of conversion of laparoscopic cholecystectomy into open cholecystectomy.

Study Design: Cross-sectional (descriptive) study

Place and Duration of Study: This study was carried out at Surgical Unit of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar for 14 months, from 1-11-2010 to 31-12-2011.

Patients and Methods: A total of 126 patients of symptomatic gallstones disease fulfilling the inclusion criteria were subjected to laparoscopic cholecystectomy and were followed through out the procedure to see for any conversion and its cause.

Results: The mean age of patients was 40.65±10.35 with range of 20-65 years. The total no of cases converted to open cholecystectomy were 11 out of 126. Thus frequency of conversion was 11 equal to 8.7%, with commonest cause being adhesions 9 out of 11 converted cases followed by hemorrhage 2 out of 11 conversions. Moreover conversion was more in male patients. 20.8% as compared to 5.9% in females.

Conclusion: Laparoscopic cholecystectomy is the gold standard treatment modality in the management of symptomatic gallstones disease. Its one disadvantage is the conversion into open procedure. But conversion should not be considered as complication of the procedure rather it is mature decision by the surgeons to avoid unnecessary lengthening the duration of surgery once they encounter any difficulty or interoperative complication.

Key Words: Laparoscopic cholecystectomy, Gall stone, Conversion, Cholelithiasis

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INTRODUCTION

Cholelethiasis is a common disease with a prevalence of 10-15% in the USA and about 16% in Pakistan.[1,2] Patients mostly remain asymptomatic but symptoms appear when any complication develops.[3] Ultrasonography is most useful investigation for diagnosing the gall stones or its complications like cholecystitis.[4] Symptomatic gall stone disease can end up with its complications without prompt surgical intervention. Carl-Langenbuch performed 1st successful cholecystectomy by open technique which remained the goal standard for the management of gall stones for about a century.[5] Then Philippe Moret brought a new advancement in its management by performing first successful cholecystectomy through laparoscopic technique.[6] It has become the most common major abdominal procedure performed in Western countries.[7]

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Laparoscopic cholecystectomy is preferable over open cholecystectomy for its lesser duration of hospital stay, lesser mortality and morbidity, early return to work and better cosmetic results.[8] It is also considered for management of acute cholecystitis now a days.[9] Laparoscopic cholecystectomy (LC) remains an extremely safe procedure with a mortality rate of 0.22-0.4%. Major morbidity occurs in approximately 5% of patients.[10] Laparoscopic cholecystectomy is having certain disadvantages like its conversion into open cholecystectomy. According to some studies its conversion rate is 16-18%.[11,12] Common causes for conversion mentioned in literature are dense adhesions 66.6%, common bile duct injury 22.3%, gut injury 11.1%[13] and haemorrhage 50%.[14]

The rationale of this study was that it will provided our local statistical data about frequency and common causes of conversion of laparoscopic cholecystectomy into open cholecystectomy, where adequate expertise is in the phase of development. By this study we have come to know that our results are comparable with national and international studies, which has reflected the level of our expertise in the field of laparoscopic surgery

MATERIALS AND METHODS

This cross-sectional (descriptive) study was conducted in Surgical Unit of Postgraduate Medical Institute, Lady Reading Hospital, Peshawar over a period of 14 months from 01-11-2010 to 31-12-2011. All patients aged ≥14 years (because patients <14 years of age are being dealt in paediatric surgery unit) and cholelithiasis undergoing laparoscopic cholecystectomy were included. Patients who have choledocholithiasis, empyema gall bladder, previous abdominal surgery, cirrhosis liver and gall bladder mass were excluded from the study. The cholelithiasis was diagnosed on the bases of episodes of pain and tenderness at right hypochondrium aggravated by taking fatty meal and ultrasound abdomen suggestive of gall bladder stones. All the patients with diagnosis of cholelithiasis fulfilling the inclusion criteria were admitted either through OPD or casualty. After taking informed consent for study and surgery, detailed history was taken and clinical examination was performed. Preoperative investigations included full blood count, random blood sugar, viral serology, blood urea and serum creatinine, chest x ray, ECG. Ultrasound scan abdomen and liver function tests were performed in all cases in order to confirm the diagnoses and rule out associated complications. Then all the patients were be kept nil by mouth from 12:00 mid night before surgery. Pre operative antibiotics were given at the time of induction of anesthesia and patients were followed throughout the procedure to look for conversion if any and its cause such as adhesions, common bile duct injury, hemorrhage & gut injury. All the information and other demographic features of the patients were recorded in a pre designed proforma. Laparoscopic cholecystectomies were performed by the same surgeon with 5 years experience of laparoscopic surgery blinded from the details and inclusion of the patients in the study.

RESULTS

Out of 126 patients, 102 (81%) were women and 24 (19.3%) were men. The mean age was 40.65±10.35 yrs and age range of 20-65 yrs. Study population largely comprised of female patients of relatively younger age group. Eleven 11 (8.7%) patients required conversion to open procedure. Thus the rate of conversion was 8.7%. Commonest cause being adhesions 9 out of 11 (7.1%) converted cases followed by haemorrhage 2 out of 11 (1.6%) conversions. Moreover conversions were more in male patients 20.8% as compared to 5.9% in females (Tables 1-2).

Table No.1: Conversion of laparoscopic cholecyst-ectomy into open cholecystectomy

Conversion	No.	%
Yes	11	8.7
No	115	91.3
Total	126	100.0

Table No.2: Gender-wise distribution of patients (n=126)

Gender	Conversion	No.	%
Male	Yes	5	20.8
	No	19	79.2
	Total	24	100.0
Female	Yes	6	5.9
	No	96	94.1
	Total	102	100.0

DISCUSSION

Symptomatic gall stone disease can end up with its complications without prompt surgical intervention. Cholecystectomy was performed by open technique for management of gall stones disease which remained the goal standard for the management of gall stones for about a century.[5,15] But now this is the era of minimally invasive or key hole surgery and performing laparoscopic cholecystectomy for GBS has revolutionized its management.[16,17]

Laparoscopic cholecystectomy became an attractive treatment modality for cholelithiasis because of less scarring, shortened hospital stays, earlier return to usual activities.[18] Despite the fact that laparoscopic cholecystectomy has got many advantages but its conversion into open cholecystectomy is disappointing not only for patient but for surgeon as well. But conversion should not be considered as complication of the procedure rather it is mature decision by the surgeons to avoid unnecessary lengthening the duration of surgery once they encounter any difficulty or intraoperative complication.

The factors leading to conversion of laparoscopic cholecystectomy into open cholecystectomy have been addressed by different studies in literature and those identified so for range from age of the patient, gender, obesity, acute cholecystitis, inexperience The conversion rate of 3.6% to 13.9% is reported in literature.[23,24] The frequency of conversion in this study being presented is 11 equal to 8.7%, which is according to that mentioned in literature. Our study population was younger, mean age 40.65±10.35 years. Daradkeh[24] reported mean age of 47.2 years, whereas Bingener et al[23] 40 years.

The reported conversion rates for acute cholecystitis range from 12% to 37.5%.[25] However, the rate of conversion is high amongst studies from the Asian countries as compared to those from western world. In most cases, dense adhesion around the gall bladder and uncontrolled bleeding were the main reasons for conversion to the open procedure.[11] Also in this study commonest cause being adhesions 9 out of 11 converted cases followed by haemorrhage 2 out of 11 conversions. Moreover conversions were more in male patients. 20.8% as compared to 5.9% in females. This was similar to Ibrahim et al[15], Brodsky et a[26] and Al

Salamah[27]also found male gender as a most significant determinant for conversion to open cholecystectomy. Gharaibeh et al [28] reported 24% conversion rate in males vs. 4% in females, whereas Lim et al[29] reported 16.6% conversions in males vs 8.2% in females. Male gender is thought to be a risk factor for conversion because of either behavioral differences[30] or differences in anatomy and physiology such as volume of abdomen, hormones and fats distribution. According to some studies age is also a risk factor for conversion but in this current study age is not a risk factor for conversion, which is according to a study by Shamim et al.[31] Most conversions happened after a simple inspection or a minimum dissection, and the decision to convert should be considered as a sign of surgical maturity rather than a failure. Conversion should be opted for in the beginning and at the time of recognition of a difficult dissection rather than after the occurrence of complication.[15,16]

CONCLUSION

Laparoscopic cholecystectomy is the gold standard treatment modality in the management of symptomatic gallstones disease. Most of the laparoscopic cholecystectomy performed fall in relatively younger age group female in this study our conversion rate is comparable with national and international literature, commonest cause of conversion was adhesions. Male gender was also risk factor for conversion. On the basis of our results we may recommend laparoscopic cholecystectomy for management of symptomatic gall stone disease in our setup where adequate expertise are in the phase of development.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Proton Pump Inhibitors

Role of Proton Pump Inhibitors in Chronic Cough

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ABSTRACT

Objective: To see the effectiveness of Proton Pump Inhibitors in patients with chronic cough at Liaquat University Hospital.

Study Design: Observational study

Place and Duration of Study: This study was conducted at ENT Department, Liaquat University Hospital, Jamshoro/Hyderabad from November 2010 to October 2011.

Materials and Methods: Irrespective of age and gender 109 cases were recorded with history of chronic cough. After getting a detailed History all the cases were examined thoroughly for any pathology in Nose, Nasopharynx, Sinuses, Throat and Larynx in ENT department and then Sent to Physician to find or exclude the pathology in chest and Gastro intestinal tract. Required investigations were carried out in selected cases. All the cases after diagnosis were selected for PPI treatment for 30 days. Patient's response to the treatment was recorded. All the data regarding sign symptoms, clinical diagnosis, duration of cough and response of the cases to PPI treatment was entered on Performa for analysis.

Results: 109 cases were chosen in present study with chronic cough, majority of the cases 55/(50.45%) were found with age group of 41-60 years. Female were found in the big percentage 63/(57.79%), as compare to male 46/(42.20%), mostly 86/(78.89%) cases had duration of cough under VIII weeks. **39**/(35.77%) cases were noted with feeling of lump in throat and this was commonest symptom. 57/(52.29%) patients were found with complete response, **35**/(32.11%) patients were noted with partial response and continued for some more days, while **17**/(15.59%) patients had not respond to PPI treatment and those were advised some other investigations and treatment.

Conclusion: PPI having prime role in cases of chronic cough. PPI caneasily be given on Clinical ground even without more investigations.

Key Words: Proton Pump Inhibitors, Chronic Cough, Liaquat University Hospital

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INTRODUCTION

Chronic nonspecific cough, characterized as a non productive cough without identifiable respiratory illness or known reason.[1] Continuing for more than III to VIII wks.[2] Represents a critical weight to medicinal services expenses and impressively personal satisfaction. Gastroesophageal reflux disease (GERD) correspond to one of the three fundamental reasons of chronic cough (alongside asthma and upper respiratory cough/postnasal trickle disorder), concerned in up to 41% of chronic cough cases.[3] The clinical highlights of GERD-related cough incorporate indigestion, regurgitation, and/or compounding of cough after nourishments or medicines known to diminishing lower esophageal sphincter-pressure, with extra-esophageal indications, for example, hoarseness, wheezing, sore throat, pain of the chest, and globus likewise described. Whilst excellent GERD manifestations are occur in 6–10% of chronic cough cases, GERD is clinically quiet in up to 75% of patients with GERD-linked cough.[4] Diagnosis of GERD is often in light of the clinical reactions of cough to antireflux treatment as opposed to on target evaluations of GERD fundamentally. Besides, an expanded comprehension of the pathophysiology of GERD and specifically the particular occurrence of laryngopharyngeal reflux (LPR), has highlighted the multifaceted nature of this situation, with the requirement for individual cases appraisal and customizing of treatment getting to be obvious. Coughing may be incited by reflux through various systems. The regurgitation of gastric substance into the laryngopharynx can bring about mechanical or pH-delicate stimulation, through chronic swelling prompting the sensitization of peripheral nerves mediating cough.[5] This due to acid or nonacid (specifically, bile and pepsin) origin. It has been recommended that coughing can likewise be affected by "micro" or "noiseless" goal, brought on by the immediate initiation of tracheo-bronchial receptors by reflux entering the airway. Distal esophageal reflux might likewise induced cough due to vagal stimulation known as oesophago-bronchial reflex.[6] Ing et al.[7] showing infusing acid in throat of chronic cough cases

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developed coughing. Moreover whilst implantation of acid (contrasted with saline) into the throat of those GERD cases without chronic cough had no impact, a sharpened cough reflex to capsaicin was noted in that's GERD cases with chronic cough.[8]

An option pathophysiology is that coughing can actually be the causation in reflux: expanded intra-stomach pressure amid strenuous coughing incidents adversely affecting the lower esophageal sphincter, perhaps by method for a positive input loop.[9] Proton pump inhibitors (PPIs) are viewed as the medications of decision for acid linked illnesses as well as GERD.[10] Proton pump inhibitors (PPIs) have ordinarily been the pillar exact treatment for GERD-linked cough. A few times without history of GERD patient have a silent stimulation prompting chronic cough; these asymptomatic patients might likewise respond on PPI. Therefore purpose of this series is to assess effectiveness of PPI in cases with chronic cough at LUMHS.

MATERIALS AND METHODS

Study was performed in ENT department of LUH Jamshoro/Hyderabad in 2010-2011. Irrespective of age and gender 109 cases were recorded with history of chronic cough. All the cases having persistence cough lasting for III to VIII wks or more were selected. Patients with history of pregnancy or cardiac and pulmonary disorders, viral or fungal infections, Malignancies or Zollinger –Ellison syndrome, chronic alcohol or drug abuse and smokers, FB bronchus and patients on ACE inhibitors, patients with high grade of low grade evening rise fever and having cough with sputum, were excluded from study. After getting a detailed History all the cases were examined thoroughly for any pathology in Nose, Nasopharynx, Sinuses, Throat and Larynx in ENT department and then Sent to Physician to find or exclude the pathology in chest and Gastro intestinal tract. Required investigations like X-Ray Para Nasal Sinuses and Chest in all cases and Flexible Nasopharyngoscopy and Upper GI Endoscopy were carried out in selected cases. All the cases after diagnosis were selected for PPI treatment for 30 days. All the data regarding sign symptoms, clinical diagnosis, duration of cough and response of the cases to PPI treatment was entered on proforma, and analyze on SPSS version 16.0.

RESULTS

Total 109 patients were selected in this study with chronic cough majority of the cases 55/(50.45%) were found with age group of 41-60, 2nd most common age group was 21-40 years 35/(32.11%), while 10/(9.17%) cases were below 20 years of the age and 09/(8.25%) were above the 60 years of the age. Female were found in the majority63/(57.79%) as compare to male 46/(42.20%), mostly 86/(78.89%) cases had duration of cough under VIII weeks, while 23/(21.10%) cases were found with above VIII weeks of the duration. **Table: 1.**. Majority of the cases **39**/(35.77%) were noted with feeling of lump in throat, while Presentation as Sore throat, Post nasal drip, Retrosternal pain, Wheezing and Nocturnal regurgitation were found with percentage of **23**/(21.10%), **27**/(24.77%),**28**/(25.68%), **11**/(10.09%) and **19**/(17.4%) respectively, while **29**/(26.60%) cases were without any symptom. **Table: 2.**

After treatment 57/(52.29%), patients were found with complete response, **35**/(32.11%) patients were noted with partial response and continued for some more days, while **17**/(15.59%) patients had not respond to PPI treatment and those were advised some other investigations and treatment. **Table:3.**

Table No.1: Demographic characteristics of the cases. n= 109

Characteristics	#of cases/%
AGE GROUPS	
< 20	10/(9.17%)
21-40	35/(32.11%)
41-60	55/(50.45%)
> 60	09/(8.25%)
GENDER	
Male	46/(42.20%)
Female	63/(57.79%)
DURATION OF COUGH	
3-8 weeks	86/(78.89%)
More than 8 weeks	23/(21.10%)

Table No.2: Associated features of the cases n= 109

Features	#of cases/%
Sore throat	23/(21.10%)
Post nasal drip	27/(24.77%)
Retrosternal pain	28/(25.68%)
Wheezing	11/(10.09%)
Feeling of lump in throat	39/(35.77%)
Nocturnal regurgitation	19/(17.4%)
No other symptom	29/(26.60%)

Table No.3: Response of the cases to PPI n= 109

Response	#of cases/%
Complete responder	57/(52.29%)
Partial responder	35/(32.11%)
Not responder	17/(15.59%)

DISCUSSION

Cough is usual symptom of many diseases which is usually simple to diagnose but sometime it may become troublesome so that to exclude upper RTI and the chest infections also if the symptoms of GERD are marked but in some cases it is difficult due to masked effects. PPI if given in such cases proved to be an effective Drug for a symptomatic drug treatment of chronic cough. In this study female were found in the majority, 55/(50.45%) were found with age group of 41-60, 2nd most common age group was 21-40 years 35/(32.11%),

while 10/(9.17%) cases were below 20 years of the age and 09/(8.25%) were above the 60 years of the age. Baldi F et al,[11] reported majority of females and Most of the patients were middle-aged females and 25 (55.5%)

A study conducted by Riaz et al, showed percentage of Pakistani students having weekly episodes of heart burn is significantly higher than that in general Asian population.[21] In this series majority of the cases **39**/(35.77%) were noted with feeling of lump in throat, while Presentation as Sore throat, Post nasal drip, Retrosternal pain, Wheezing and Nocturnal regurgitation were found with percentage of **23**/(21.10%), **27**/(24.77%),**28**/(25.68%), **11**/(10.09%) and **19**/(17.4%) respectively.

D'Urzo A et al.[12] reported chronic cough is highlighted in GERD and unique side effect in up to 75% of patients. Adults having microaspiration, cough takes after manifestations of indigestion, disgorging, sour tast, pain of throat and hoarseness. In another study demonstrate that chronic cough was brought about by reflux in 21% patients. Moreover, the analysts demonstrated that constant hack was the sole displaying indication in GERD 43% of the time.[13] Otitis media might likewise be connected to GERD.[14]

Loehrl TA et al,[15] looking at otitis media with radiation in grown-ups exhibited that pepsinogen fixation was higher in center ear emission in patients who reported GERD manifestations, furthermore, treatment for GERD with PPIs gave a few cases with GERD symptom relief as well as decreasing the concentration of pepsinogen in the effusion. Also, research has demonstrated that cases having chronic rhinosinusitis have an expanded incidence of GERD, these chronic ceaseless rhinosinusitis manifestations in numerous patients are decreased after GERD treatment.

Frequently, they display as hoarseness, recurrent throat passing, a postnasal trickle, abundance mucus, sore throat, a globus sensation, dyspnesia, or cough. Chronic laryngitis and sore throat are connected with GERD in upwards of 60% of cases.[16] likewise; one study demonstrated that no less than 50% of patients giving laryngeal and voice issue had laryngopharyngeal reflux.[17] Less-regular GERD- linked laryngopharyngeal issue incorporate paroxysmal laryngospasm, subglottic stenosis, vocal-string granuloma, and cancer of the larynx and pharynx.[18]

After treatment 57/(52.29%), patients were found with complete response, **35**/(32.11%) patients were noted with partial response and continued for some more days, while **17**/(15.59%) patients had not respond to PPI treatment and those were advised some other investigations and treatment. Baldi F et al,[11] demonstrated that more than 80% of the patients those had full relief in cough on complete treatment and demonstrate the good response to PPI test. Several studies showed when chronic cough treated with PPIs 26%-43% patients got good relief.[19,20]

CONCLUSION

We concluded that PPI having prime role in cases of chronic cough. PPI can easily be given on Clinical ground even without more investigations. Patients with Chronic Pharyngitis responded well on antimicrobials with addition of PPI. All the physician and ENT specialist should understand the GERD on the time cough treatment. More research is required for complete effectiveness of PPI in the cases with chronic cough.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

To Detect the Fungal Infection in the Patients with Nasal Polyps

Fungal Infection in Nasal Polyps

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ABSTRACT

Objective: To determine the prevalence of fungal infection in the patients having nasal polyps at Liaquat University Hospital, Hyderabad.

Study Design: Observational and prospective study

Place and Duration of Study: This study was conducted in the Department of the ENT of Liaquat University Hospital, Jamshoro/Hyderabad from March 2012 to August 2012.

Materials and Methods: Total 50 had selected. All the cases with nasal polyp, both genders and above 18 years of the age were integrated. Routine lab investigations had completed. Radiological examination including the X-ray of paranasal sinuses and CT scan had done to diagnosis sinuses, bony erosion, orbital and intracranial extension. Surgical procedure had done according to the need of the patient. After surgery all the samples separated in 2 places under sterile process. One for histopathology and 2nd in the normal saline had sent for fungal Culture of specimen.

Results: Total 50 cases were selected in the study after diagnosis of nasal polyp, mean age of the cases was mean +SD=36.05+7.21 years, male had found in the majority 31/(62.0%). Nasal obstruction was the most common 42/(84.0%) in the clinical presentation. Majority of the cases 26.0% were undergo went surgical procedure of nasal polypectomy. After done histopathology frequently diagnosis found as Inflammatory polyp 43/(86.0%), while **08**/(16.0%) cases were found with fungal infection and 42/(84.0%) were without fungal infection after culture test.

Conclusion: In conclusion fungal infection is found most common in the cases having nasal polyps.

Key Words: Nasal polyp, fungal infection, Liaquat University Hospital

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INTRODUCTION

Nasal polyposis is extremely commonest ailment of the nasal hole with the occurrence of (1.4%) and commonest in adults as contrast with the children.[1] It is accepted that nasal polyps are framed as a consequence of continuous nearby swelling of nasal or sinus mucosa, that's developed by expanding sub mucosal edema and afterward open to airway. On the other hand, the fundamental development of the nasal polyp is not understand accurately.[2]

Essential symptoms of NP are nasal blockage and congestion, hyposmia or anosmia and if connected with chronic sinusitis a purulent nasal release. Supplementary symptoms involve are, post nasal drip, rhinorrhea, facial pain and aggravation in the sleeping.[3] several series considered that polyps to be extreme appearance of chronic swelling, consequently, conditions prompting chronic inflammation in cavity of nose can develop nasal polyps.[4] Nasal location of mucosal injury can cause pooling of mucus and following colonization by fungus.[5] fungal components were associated to be the causative elements of chronic rhinosinusitis and fungal etiology had found to underlie extreme NP. Fungal agents separated from paranasal sinuses incorporate Aspergillus, Mucor, Histoplasma, Coccidiodies, Candida,[6] Acremonium, Curvularia, Fonsecaea , Penicillum.[7] Aspergillus spp. is the most widely recognized colonizers of sinuses.[5] Mostly fungi find out in dust, soil, air and plants. They stick to dust elements and are breathed in and placed on the nasal and paranasal sinus mucosa. Warm, clammy environment of the URT is a perfect situation for the multiplication of this organisms,[8] though; that's infrequently pathogenic causing host resistance is high with the exception of under positive development situations in extremely responsive individuals.[2] Cause or effects of the fungal infection in the nasal polyps is hard to focus due to the omnipresent quality of fungal spores. At the same time, several studies demonstrate that these polyps might likewise be created due to fungal infection of sinunasal mucosa.[9] Hence NP arrangement and development may be start by both fungal infection and non infectious swelling.[10,11] Fungal infection and local allergic method of colonization of sinunasal mucosa had impact in NP development. Nasal fungal infection and paranasal sinuses are arranged in 2 parts as, (intrusive) and (non obtrusive). Non intrusive incorporates mycetoma and hypersensitive fungal sinusitis. Intrusive contains the unending sluggish structure, that shows gradually dynamic bone erosion, and fulminate appearance.[12] Purpose of this study to determine the number of the cases involved in fungal infection from the cases of

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nasal polyposis at Liaquat University Hospital Hyderabad.

MATERIALS AND METHODS

This observational and prospective study had done in Department of the ENT of LUH Hyderabad. With six month of duration from March 2012 to august 2012. Total 50 cases had selected. All cases having nasal polyp, both genders and above 18 years of the age were integrated. All the patients with previous surgical history of the nasal polyposis, nasal structural abnormalities, severe co morbidities and pregnant women had excluded. After taking an informed written consent, details of history, through clinical examination by the ENT surgeon. Face examination had done to see the apparent deformity "face swelling in the sinus region, cheek, and nasal deformity". Examination of Nose and throat was done to diagnose the nasal obstruction effects. Routine laboratory investigations were completed. Complete radiological diagnosis had done as paranasal sinuses X-ray and CT scan to diagnose sinuses, extension of the orbital and intracranial and bony erosion,. Surgical procedure was done according to the need of the patient. After surgery samples had separated in two places under process of sterilization. One was sent for histopathology and 2nd had been sent for fungal Culture of specimen. Data had analyzed on SPSS version 16.0.

RESULTS

Total 50 cases were selected in the study after diagnosis of nasal polyp, mean age of the cases was mean +SD=36.05+7.21 years, male had found in the majority 31/(62.0%) as compare to female 19/(38.0%), majority of the cases was multiple work performer such as labrour 17/(34.0%), while House wife, Farmer, Teacher, Driver and Shopkeeper were 11/(22.0%), 07/(14.0%), 04/(8.0%), 08/(16.0%) and 03/(6.0%). Table 1.

Nasal obstruction was the most common 42/(84.0%) in the clinical presentation, while Nasal deformity in 11/(22.0%) cases, Headache in 23/(46.0%) cases, Sneezing in 15/(30.0%), Sore Throat in 17/(34.0%), Blood discharge from nose in 05/(10.0%) and Sinus swelling in 20/(40.0%) cases, while Difficulty in speaking was found only in 01/(2.0%) of the cases. Mostly patients were found 1 to 2 years of duration illness, results shows in Table 2**.**

Majority of the cases 26.0% were under went surgical procedure of nasal polypectomy, while 18.0% patients were underwent C.W.L operation and only 6.00 of the cases were underwent lateral rhinectomy. Figure 1.

After done histopathology frequently diagnosis found as Inflammatory polyp 43/(86.0%), while **08**/(16.0%) cases were found with fungal infection and 42/(84.0%) were without fungal infection after culture test. Table 3.

Table No.1: Basic features of the cases. n= 50

Characteristics	#of Cases/%
Age	
mean +SD	36.05+7.21 years
Gender	
Male	31/(62.0%)
Female	19/(38.0%)
Ocupational Status	
House wife	11/(22.0%)
Farmer	07/(14.0%)
Teacher	04/(8.0%)
Driver	08/(16.0%)
Shopkeeper	03/(6.0%)
Multiple work performer	17/(34.0%)

Table No.2: Clinical pattern of the cases. n= 50

Features	#of cases/%
Nasal Obstruction	42/(84.0%)
Nasal deformity	11/(22.0%)
Headache	23/(46.0%)
Sneezing	15/(30.0%)
Sore Throat	17/(34.0%)
Blood discharge from nose	05/(10.0%)
Sinus swelling	20/(40.0%)
Difficulty in speaking	01/(2.0%)
Illness Duration	
> 1 year18	18/(36.0%)
1 – 2 years17	17/(34.0%)
3 - 4 years10	10/(20.0%)
< 4 years05	05/(10.0%)

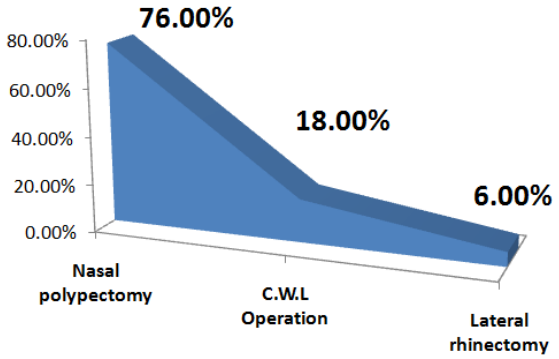

Figure No.1: Distribution of surgical procedure in the cases. n= 50

Table No.3: Histopathological and fungal culture findings. n= 50

Response	#of cases/%
Inflammatory polyp	43/(86.0%)
Stromal Atypia	02/(4.0%)
Fibrotic	02/(4.0%)
Others	03/(6.0%)
Fungus culture	
Positive	08/(16.0%)
Negative	42/(84.0%)

DISCUSSION

Nasal polyps start from respiratory mucosa cover up multiple part of ethmoidal bones. It has been proposed that NP development increments with age.[13,14] Settipane mentioned that NP incidence achieves a top in patients with age of 50 years or above,[14] besides, he mentioned that asthmatics more than 40 years old are four times more involve in NP than under the 40. Furthermore, he reports that asthmatics over 40 years of age are four times more likely to have NP than those under 40. In France, the assessed frequency of nasal polyposis expanded with age, coming to a top in the 50 to 59 year age.[15] In another study in France the mean age was 49.4 ± 17.6.[16] In this series total 50 cases were selected in the study after diagnosis of nasal polyp, mean age of the cases was mean +SD= 43.05+7.21 years, male had found in the majority 31/(62.0%) as compare to female 19/(38.0%).

Nasal polyposis has an extraordinary effect on patients' quality of life, and brings social and the limitation of occupation. It affects vitality and the general health, and mental health is more affected than physical health.[17] In this series majority of the cases was multiple work performer such as laborers 17/(34.0%).

Haro JI et al[18] reported that the main clinical manifestation was nasal obstruction in 100% of the patients, followed of nasal pruritus with 62%, sneezing in 60%, anterior rhinorrhea in 50%, posterior rhinorrhea in 32% and hyposmia/anosmia in 20% of the patients.

Meymane Jahromi A et al,[19] demonstrate that nasal polyposis affects men (60.3%) more frequently, at a mean age of 39.5 years. Nasal blockage was the commonest symptom (81.1 %) followed by rhinorrhea (37.7%). Similarly in our results nasal obstruction was the most common 42/(84.0%) in the clinical presentation, while Nasal deformity in 11/(22.0%) cases, Headache in 23/(46.0%) cases, Sneezing in 15/(30.0%), Sore Throat in 17/(34.0%), Blood discharge from nose in 05/(10.0%), and Sinus swelling in 20/(40.0%) cases, while Difficulty in speaking was found only in 01/(2.0%) of the cases. Newton JR et al.[20] suggested that the main symptoms found nasal obstruction, and obstruction is generally constant, by it may vary depending upon the size and region of the polyps

Farrukh M SH et al[21] showed that 73.3% patients with nasal polyp underwent nasal polypectomy, 20.0% cases intra nasal ethmoidectomy and 6.6% patients under went extra nasal ethmoidectmy. Similarly in this series majority of the cases 76.0% were under went surgical procedure of nasal polypectomy, while 18.0% patients were underwent C.W.L operation and only 6.05 of the cases were underwent lateral rhinectomy. The individuals who had more commonness of growths in their nasal polyps had quite a while introduction to clean at work or in their home. More incidence of fungal infection found in nasal polyps those having long time revelation to dust. Greval et al.[22] reported 10.7% patient suffering from fungal sinusitis. Dall'Igna et al.[23] (2005) reported 6.7%. Garg et al.[24] (2013) reported 26.6%. While in this series **08**/(16.0%) cases were found with fungal infection after culture test.

CONCLUSION

In conclusion fungal infection is found most common in the cases having nasal polyps, relevance of the fungi research is required and the immune system investigation is very necessary in cases having nasal polyposis, to accurate treatment.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Comparative Study of Olopatadine Hydrochloride 0.1% and Emedastine difumarate 0.05% Comparing their Clinical Efficacy and Adverse Effects in Allergic Conjunctivitis

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ABSTRACT

Objective: To assess the efficacy and adverse effects of 0.1% Olopatadine hydrochloride (OHC) and compare them to 0.05% Emedastine difumarate (ED) in the treatment of allergic conjunctivitis.

Study Design: Prospective and comparative study

Place and Duration of Study: The study was conducted at Islam Teaching Hospital, Islam Medical College, Sialkot from February 2013 to June 2014.

Materials and Methods: 74 adult patients including 35 male patients aged 21- 47 years (Average 32.39) and 39 females aged 20 - 42 years (Average 31.8) some with a history of systemic allergic manifestation (e.g. asthma, dermatitis, or bronchitis) along with sign and symptoms of allergic conjunctivitis were enrolled in the study. At the time of induction, manifestations of allergic conjunctivitis (mucous discharge, itching, conjunctival congestion, chemosis, and watering) were present. Patients were allocate at random to either of the 2 groups, A and B. The patients in the Group A, (n = 36) received OHC and those in the Group B (n = 38) were treated with ED. The dose in Group A was one drop in both the eyes 12 hourly. Group B received one drop in both the eyes 6 hourly. The study was started on the first patient visit, when after the diagnosis; the drug was administered. Patients from both the groups were re-evaluated half an hour, forty eight hours, seven and fourteen days later. Efficacy and side effects in both the groups were assessed. The severity of signs and symptoms were assigned a score from 0 - 3. The results were analysed using independent sample T test.

Results: At the start of the study, cumulative score of the patient's sign and symptoms was calculated, with a mean value of 7.31 for group A and 7.38 for group B. There was no significant statistical disparity between the groups (p = 0.88). The cumulative scores at the end of study on day fourteen were 0.72 for group A and 1.0 for group B. This was also statistically not significant (p = 0.15) but Olopatadine was noted to be more effective.

The side effects of both the medicines were similarly assessed with cumulative scores calculated at each follow up. In group A, there were minimal side effects with mean cumulative score on the final visit was 0.25 in group A and 0.54 in Group B, with statistically significant (p = 0.015) difference.

Conclusion: Olopatadine was discovered to have better efficacy (not statistically significant) and less adverse effects (statistically significant) than Emedastine.

Key Words: Olopatadine, Emedastine, Allergic Conjunctivitis

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INTRODUCTION

Allergic conjunctivitis (AC) is an immune mediated ocular surface disorder that disturbs nearly one fourth of population at large[1,2]. Of the various causes of conjunctivitis, allergy is the most common aetiology, responsible for 15% to 40% of the presentations with conjunctivitis[3]. The incidence rises in spring and summer[4]. Allergic conjunctivitis is the inflammatory response of the conjunctiva to environmental antigens such as animal dander, pollen, and dust etc. Redness and itching are the most consistent symptoms[3]. AC is an immune mediated disorder. It is a "Type I hypersensitivity reaction" to pollen and other antigens, arbitrated by IgE as indicated by accompanying eosinophilia, and results from a sequence of biological reactions[5]: a) atmospheric allergens cause sensitization; b) activation of mast cells by IgE and subsequent

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release of mediators; c) inflammation of the conjunctiva with prevalence of eosinophils; d) production of cytokines, and e) exaggerated production of mucous.

Mast cells have a major role in this pathophysiology[6]. These cells' action not just contributes to the progression of this acute hypersensitivity reaction but also plays an important role in the metabolic regulation of response of connective tissue succeeding this occurrence in the form of fibrosis. After the exposure to allergen, in both, acute and chronic phase, one of the key features is the appearance of inflammatory cells (neutrophils, lymphocytes, and eosinophils) in lacrimal secretion within nearly six to twenty four hours. Histamine is the main mediator, responsible for the sign and symptoms associated with allergic conjunctivitis[7,8]. Key signs comprise conjunctival hyperaemia, conjunctival chemosis, watering, mucous production, and papillae. Major and frequent presenting complaints comprise of itching, watering, blurry vision photophobia and foreign body perception. Itching is the hallmark of AC. AC can be managed with local anti-allergic drugs such as anti-histamines. These may be solo or in formulation with α-adrenergic drugs[9]. The management of allergic conjunctivitis has markedly evolved in recent times[10-13]. The vast array of treatment options provides opportunities for more individualized therapy, but at the same time also leaves the physicians and patients confused over which option to adopt[14]. Antihistamines delivered topically are the most favoured option for the management of allergic conjunctivitis[15]. These agents inhibit the effect of histamine on H_1 receptor. Emedastine difumarate (E.D) 0.05% is an antagonist with very selective and more potent H_1 receptor affinity when compared to levocabastine and other agents like ketotifen[16]. The latest type of topical agents for management of allergic conjunctivitis have the dual - effect, a strong antihistaminic activity that provides rapid relief and mast-cell stabilization that are responsible for extended respite[9]. Drugs such as Olopatadine, bepostatine, epinastine and azelastine are counted in in this group. Amongst this group Olopatadine hydrochloride (O.H.C) inhibits stimulation of eosinophils, macrophages and neutrophils, hence reducing liberation of platelet-activating factors, leukotrienes and other mediators of inflammation[14]. O.H.C 0.1% has a fast onset of action, initiating within a few minutes and lasting for hours, hence allowing a twice daily dose. It has potent, choosy antihistaminic and mast cell stabilizing activity[17].

MATERIALS AND METHODS

The study was conducted at Islam Teaching Hospital, Islam Medical College, Sialkot from February 2013 to June 2014. This was randomized double blind prospective study with active treatment concurrent control[18].

74 patients were included in the study, of these, 11 had a history of systemic manifestations of allergy, which included Allergic rhinitis, asthma, and dermatitis. Patients using any drugs at the time of the study were excluded as were those who had undergone ocular surgery in recent past. Females in whom pregnancy could not be ruled out were also excluded. All the patients were exhibiting clinical features of allergic conjunctivitis (Figure 1).

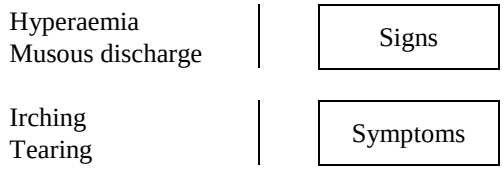

Figure No.1: exhibiting clinical features of allergic conjunctivitis

These symptoms and signs were classified in 4 grades: "Grading for Hyperemia: 0, Absent; 1, Mild: little dilatation of blood vessels, pink color, distributed in quadrants; 2, Moderate: moderate size dilatation of blood vessels, generally red color, generalized and randomly located in conjunctiva; 3, Severe: Numerous generalized dilatation of blood vessels, red color with or without chemosis. Grading for Mucous discharge: 0 , Absent 1; Mild: small mucous conglomerates, preferably concentrated in the inferior cul- de-sac; 2, Moderate: Bigger mucous conglomerates in the inferior conjunctival cul-de-sac, producing discomfort generally in the morning; 3, Severe: Big mucous conglomerates in cul-de-sac with discharge in palpebral edges and at the caruncle level, accompanied with sticky eyes in the morning. Grading for Itching: 0, Absent; 1, Mild: infrequent, with tendency to scratch or rub the eyes; 2, Moderate: constantly there, with tendency to scratch or rub the eyes; 3, Severe: continuous, frequently rubbing the eyes; Grading for Tearing: 0, Absent; 1, Mild: infrequent; 2, Moderate: perceived by patient, felt as discomfort; 3, Severe: permanent and commonly accompanied by drying of the eyes and palpebral edges".

Subjects were separated into 2 groups (A and B) comprising of 36 and 38 members respectively. The first group (Group A) was treated with 0.1% Olopatadine hydrochloride (OHC) and the second group (Group B) comprised those who received Emedastine difumarate 0.05% (ED). Every subject was administered a single drop in each eye every twelve hours, in group A and 6 hourly in group B. At the initial visit, the patients sign and symptoms were recorded and the first drop of medication was instilled in both the eyes. Patients were then re-evaluated after an interval of thirty minutes and any adverse effect / discomfort was noted as well as any improvement in the sign and symptoms. The next visits were after 48 hours, 1 week and 2 weeks respectively.

Adverse reaction/intolerance was noted and graded according to the following criteria:

"Grading for Burning/ foreign body perception: 0, Absent; 1, Mild: mild burning/stinging or foreign body perception upon administration of drops; 2, Moderate: mild burning/ stinging or foreign body perception at instillation which persisted; 3, Severe: significant burning/stinging or foreign body perception at instillation that persisted to the point that therapy had to be withdrawn. Grading for Blurring of vision and dryness of eyes : 0, Absent; 1, Mild; 2, Moderate; 3, severe".

The symptoms and signs were assessed at before treatment and then thirty minutes, forty eight hours, seven days and fourteen days after commencement of therapy:

Statistics: The results were analysed using independent sample T test.

RESULTS

Members of group A (OHC) when evaluated half an hour after the first dose, showed an overall improvement in the symptoms. However, there was no improvement in the amount of discharge. 4 patients were excluded from the study on day 7 (due to no response), the rest completed the study. No adverse effect, except mild dryness, were witnessed (4 - 6%).

In Group B (ED), 6/38 of the subjects were excused from the study at day 7 of commencement of therapy because of the lack of a positive response. A further 3.13 % of the patients (1/32) missed further follow up. The patients reported mild side effects of stinging and burning as well as foreign body sensation at various points in the study; however, they were not strong enough to cause a withdrawal or discontinuation of therapy.

At the start of the study, pre-treatment cumulative score of the patients sign and symptoms was calculated, with a mean value of 7.31 for group A and 7.38 for group B. There was no significant statistical disparity between the groups (p = 0.88). The cumulative scores at the end of study on day fourteen were 0.72 for group A and 1.0 for group B. This was also statistically not significant (p = 0.15) but Olopatadine was noted to be more effective (Table 1).

Table No.1: Comparison of Cumulative score of sign and symptoms

.	Cumulative Score		p Value
	Group A (OHC)	Group B (ED)	
Pre-treatment	7.31	7.38	0.88
30 minutes	5.94	6.0	0.78
48 hours	4.28	4.45	0.78
7 days	2.25	2.51	0.63
14 days	0.72	1.0	0.15

The side effects of both the medicines were similarly assessed with cumulative scores calculated at each follow up. In group A, there were minimal side effects with no stinging/burning sensation or blurring of vision. The only side effect noted was mild dry eye in a small number of patients. The mean of cumulative score on the final visit was 0.25 in group A. Group B patients reported side effects including, stinging, burning, foreign body sensation as well as mild dry eye. However, none of these was severe enough to cause withdrawal of the drug or cessation of treatment. The mean cumulative score was 0.54. This was found to be statistically significant (p = 0.015) (Table 2).

Table No.2: Comparison of Cumulative score of adverse effects

	Cumulative Score		
	Group A (OHC)	Group B (ED)	p Value
30 minutes	0.25	0.81	< 0.001
48 hours	0.3[illegible]	0.81	0.004
7 days	0.[illegible]	0.74	0.012
14 days	0.[illegible]5	0.54	0.015

DISCUSSION

This is a novel study comparing clinical efficacy of Olopatadine hydrochloride 0.1% and Emedastine difumarate 0.05% and their adverse effects in allergic conjunctivitis

Olopatadine is a newer, dual action agent that exerts anti-histaminic and mast cell stabilizing effect. Several studies have found Olopatadine to be very well tolerated and these results are confirmed by the present study[19,20].

The most frequent and prominent side effect encountered in the group using Olopatadine was dry eye, but since the medication was preserved, it is not possible to say if the effect was directly due the active ingredient or the preservative, as the use of preserved eye drops is associated with a high incidence of dry eye symptoms[21].

Emastidine is a potent antihistamine that results in prompt resolution of symptoms and signs, but has been found to have several side effects, including stinging and foreign body sensation. This makes the drug less preferred by a lot of patients when compared with Olopatadine.

CONCLUSION

Olopatadine was discovered to have better efficacy (not statistically significant) and less adverse effects (statistically significant) than Emedastine.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Eruption of Premolars

Eruption Time of Premolars in Children at Urban Schools of Lahore, Pakistan

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ABSTRACT

Objective: The purpose of this study was to ascertain mean eruption ages of premolars in local school children and to compare with other population groups.

Study Design: cross sectional study

Place and Duration of Study: This study was conducted in the Deptt. Of Oral Maxillofacial Surgery, KEMU, Lahore from 17.12.2009 to 17.12.2010.

Materials and Methods: The mean eruption ages of permanent teeth were derived from a cross sectional study of 4000 public and private schools children in Lahore with ages ranged 8-13 years. Children were from all classes of socioeconomic status. Sample was examined in good torchlight and emergence through the gingivae was noted.

Results: Maxillary premolars erupted earlier than the mandibular ones in both genders. The mean sequence of eruption in upper and lower arch was P_1, P_2. Maxillary 1st premolar was the first tooth to erupt in boys and girls; whereas mandibular 2nd premolar was the last one.

Conclusion: (1) The premolars erupted slightly earlier than the standards used in our practice of text books. (2) Maxillary premolars erupted earlier than mandibular premolars. (3) Local standards should be applied while planning preventive and interceptive orthodontic measures and treatment modalities in other specialties.

Key Words: Eruption, sequence, emergence, maxillary 1st premolar, 2nd premolar, Mandibular 1st premolar, 2nd premolar.

Citation of article: Iqbal J, Warraich RA, Qamar R. Eruption time of premolars in Children at urban schools of Lahore, Pakistan. Med Forum 2015;26(5):29-32.

INTRODUCTION

Eruption is a process of tooth development from bone to the stage when tooth enters in mouth and becomes clinically visible.[1] Typically, humans have 20 primary and 32 permanent teeth that erupt at different times in people. There exists a general eruption time line.[2] Primary teeth erupt into the mouth from around 6 months until the age of 2 years. These teeth are then replaced by their permanent succedaneuos teeth that begin to erupt at 6 years of age.[3] Variations in timing and atypical sequence of eruption usually correlated with genetic factors.[8] This view was supported by high inter correlation of tooth formation, between the identical twins from same zygote, compared to fraternal twins from two ovums.[9] Several authors have reported that genetic differences in permanent tooth eruption occur not only between individuals but also between population groups.[10-15] Also vast evidence exists for the racial differences.[9,16] A number of non aborigines erupted their permanent teeth earlier than Australians aborigines, whereas European or North American whites erupted later. Age standards of permanent teeth eruption currently used in Pakistan are based on norms of other countries which should not necessarily applied in our region. This knowledge of ages and sequence of eruption at which individual teeth erupt in a given ethnic group are essential for planning preventive measures, and treatment of malocclusion.[17-19] No information is available regarding the eruption chronology of local children. Therefore this study was conducted to acquire accurate eruption parameters of premolars in our region.

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MATERIALS AND METHODS

Total subjects were 4000 from different private and public schools of Lahore. There were 1969 males and 2031 females. The personal details of children were recorded from school birth registers that contained date of examination, name, date of birth, school name and sex column. The Lahore is one of the 2nd big city of Pakistan; because of job opportunities, population comprises of various parts of country.

Selection Criteria: A tooth was considered erupted when any part of its crown had pierced the Gingivae and visible in oral cavity.

Inclusion Criteria; Age range 8-13 years. All clinically healthy children with normal height and weight

Exclusion Criteria: Children excluded were like those having craniofacial or skeletal deformities, cleft lip and palate or developmental syndromes

Examination : Each child was examined by torch with the help of disposable mirror for the clinical visibility

of premolars. Findings were recorded manually in the designed Performa.

Study Design: This study was cross sectional. The ages of children were calculated from their birth date to date of examination. The calculation was done in years, more than fifteen days were taken as a whole month. Data was distributed into age groups for eruption frequency in boys and girls. Mean ages of erupted premolars were calculated.

Statistical Analysis: The data was entered and analyzed by using Statistical Package of Social Sciences (SPSS) version 18. The qualitative data like gender was presented in form of pie chart. The quantitative data has been presented in frequency table (%). Whereas mean eruption age ± SD along with S.E, and 95% confidence interval (CI), of quantitative data calculated.

Normality of quantitative data was checked by using one Sample Kolmogrove Simirnove test.

RESULTS

Total sample size 4000. Their ages ranged 8 -13 years. According to our objectives we screened the children whose lower and upper 1st and 2nd pre-molars were erupted. There were 1969 (49.2%) males and 2031 (50.8%) females. Male to female ratio was 0.96:1. (Figure 1)

The mean eruption age of lower first and second premolar was 10.21+- 1.30 and 10.63+- 1.28 years respectively. Moreover the mean eruption age of upper first and second premolar was 10.13+-1.30 years and 10.44+-1.33 years respectively.(Table 1)

There were 1604 children (872 males and 732 females) whose lower first premolar was erupted. There were 838 children (476 males and 362 females) whose lower second pre-molar was erupted. There were 1842 children (1024 males and 818 females) whose upper first pre-molar was erupted and second upper pre-molar was erupted in 1092 children (604 males and 488 females). (Table 2)

Table 3 & 4 present the Eruption of Maxillary and Mandibular 1st premolar was seen earlier in Pakistani population than English as compared to eruption ages of children in American, Hong Kong, Chinese, Iraqi, Kenyans and Zulu Negros. Maxillary 2nd premolar eruption was earlier than the English, Americans and Iraqi population group. Mandibular 2nd premolar erupted earlier in our population than in English, American, Chinese, Iraqi and Kenenyen Asian while later than Kenyan Africans and Zulu Negro population.

Table No.1: Mean Eruption age (years) of Lower/ Upper 1st and 2nd Pre-Molar

		L1PM	L2PM	U1pm	U2PM
N		1604	883	1842	1092
Mean Age (years)		10.21	10.63	10.13	10.44
S.D		1.30	1.28	1.30	1.33
S.E		0.046	0.06	0.04	0.05
95% C.I	Lower Bound	10.12	10.51	10.05	10.33
	Upper Bound	10.30	10.76	10.21	10.55
Minimum		8	8	8	8
Maximum		13	13	13	13

Table No.2: Frequency Table of Age (years) of Eruption of Lower/ Upper 1st and 2nd Pre-Molar

Age Groups (Year)	L1PM	L2PM	U1PM	U2PM
1. (8-8.99)	160	52	198	114
2. (9-9.99)	338	98	416	128
3. (10-10.99)	446	230	528	300
4. (11-11.99)	400	244	426	324
5. (12-13)	260	214	274	226
Total	**1604**	**838**	**1842**	**1092**

Table No. 3: The comparison of mean eruption ages of maxillary teeth various ethnic groups.

Tooth	Pakistani	American	English	Chinese	Iraqi	Kenyan	Kenyan	Zulu
P1	10.25	10.12	10.62	9.66	10.0	9.85	9.63	9.93
P2	10.58	11.00	11.33	10.62	10.85	10.89	10.45	10.36

Table No.4: The comparison of mean eruption ages of mandibular teeth of various ethnic groups

Tooth	Pakistani	American	English	Chinese	Iraqi	Kenyan	Kenyan	Zulu
P1	10.36	10.33	10.50	10.13	10.4	10.20	10.06	9.93
P2	10.75	11.20	11.43	10.96	11.2	11.01	10.05	10.45

DISCUSSION

This study established the eruption norms of upper and lower 1st and 2nd premolars in local population (both genders) of Lahore. Children examined belonged to different socioeconomic classes in private and public schools. Subjects belonged to lower, middle and upper classes. Variables like race, environmental, socioeconomic status, nutritional status and somatic growth etc have been mentioned widely in literature affecting mean eruption ages and sequences of permanent and deciduous dentition. These factor along

with many other local and systemic factors had shown the effects on mean eruption ages and emergence sequences of teeth. This kind of study has been not conducted ever before in any city of Pakistan. Although literature is full of such studies, which researched on different aspects of tooth eruption radiographically using different development quantitative methods. This does not end here different statistical methods have been used for clinical studies of mean and median ages. Therefore it was needed to research eruption chronologies and mean ages of races in Pakistan. The study will prove foundation for research lovers to establish eruption norms of Pakistani population in different areas. Thus keeping in view the limited resources and uncooperative behavior of school administration especially of private schools, this work could only established the eruption age norms of upper and lower premolars in local population. Therefore presented norms should not be assumed as representative of whole Pakistani population due to the different racial, geographical, environmental and tribal identities in our country. This needs to be researched in every nook of country.

Sequence of eruption: The classical eruption sequence in both genders taught and practiced in our country from the text books of dental anatomy. Which is of European population is as: M1, I1, I2, P1, C, P2, M2, of the upper arch whereas in lower arch: I1, M1, I2, C, P1, P2, M2. Likewise this study also followed the classical eruption sequence as: P1, P2 in upper arch whereas for lower arch was; also p1 and P2. However cross sectional studies provides only the mean sequence of eruption whereas exact order of eruption is possible through longitudinal study.

Upper & Lower premolars mean eruption age comparison with other populations: Mean eruption ages of upper and lower premolars in local population children has been compared with those of other ethnic groups is presented in Tables 2, 3 & 4. All the comparative studies referred in literature are cross-sectional except the study of English population by Kocher and Richardson.[21]

1. Eruption of maxillary 1st premolar was seen earlier in our population than English,[21] while later as compared to eruption ages of children in American,[20] Hong Kong Chinese,[22] Iraqi,[23] Kenyans[24] of Asian and African origin, and Zulu Negros.[25]
2. Maxillary 2nd premolar eruption was earlier than the English,[21] Americans,[20] Iraqi,[23] Honkong Chinese[22] and was found erupted later than the Kenyan24 African and Zulu[25] Nigro's.
3. Mandibular 1st premolar mean eruption age in our population was earlier than the English while erupted later as compared to the America,[20] Hong Kong Chinese,[22] Iraqi,[23] African[24] and Zulu[25] Negro's population.
4. Eruption of Mandibular 2nd premolar was earlier in our population than in English,[21] American,[20] Hong Kong Chinese,[22] Iraqi[23] and Kenenyen[24] Asian while later than Kenyan24 Africans and Zulu[25] Negro population.

Our results are in accordance with literature with differences of mean ages due to socioeconomic and other factors, as the circumstances among populations are different.

CONCLUSION

1. The premolars erupted slightly earlier than the standards used in our practice of text books.
2. Maxillary premolars erupted earlier than mandibular premolars.
3. Local standards should be applied while planning preventive and interceptive orthodontic measures and treatment modalities in other specialties.

Recommendations:

1. Study provided mean eruption age norms of local population, providing base line idea.
2. Local standards should be used in different disciplines of dentistry regarding the tooth eruption ages.
3. It is recommended that such studies should be conducted in different parts of Pakistan.
4. Eruption norms of deciduous and other permanent teeth should also be established in local population.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Interferon treatment in Hepatitis C

Standard Interferon in the Treatment of Hepatitis C; Response Rate in Genotypes 2 and 3 from an Area in Azad Kashmir, Towards North of Pakistan

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ABSTRACT

Objective: To assess the response rate and side effect profile of combination therapy with standard interferon alpha 2a and ribavirin in patients with chronic hepatitis C, genotype 2 and 3.

Study Design: Observational study

Place and duration of Study: This study was conducted at Saleem Medical Complex and Maryam Maternity home, Kotli, Azad Kashmir from January 2012 to December 2012.

Materials and Methods: Both male and female patients above 20 years of age with chronic hepatitis C, living in district Kotli Azad Kashmir, not treated previously, were included in the study. Viral load and genotyping were determined before initiation of treatment. Therapy was given with conventional interferon alpha 2a, 3 Million international units subcutaneously on alternate days and ribavirin 400mg tablets orally daily, for 24 weeks. PCR was repeated at the end of treatment and six months later. Clinical and lab monitoring was done at regular intervals and side effect profile was recorded.

Results: Out of 150 patients, 30 (20%) were males and 120 (80%) were females. Most of the patients were between 20-50 years of age (83.99%). End of treatment response was 82% and sustained viral response was 65.33%. Fever was the most common side effect followed by flu like symptoms. All the patients completed the treatment without any dropout.

Conclusion: The study showed a good response rate to standard interferon plus low dose ribavirin against genotype 2 and 3, with a favorable side effect profile without any drop out, indicating that it is a suitable treatment option.

Key Words: hepatitis C; genotypes 2 & 3; interferon alpha 2a

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INTRODUCTION

Hepatitis C is highly prevalent throughout the world. According to WHO, more than 130 million people are infected worldwide and incidence of new cases is 3-4 million per year[1,2,3]. The high prevalence rates are found in Africa (5.3%), Eastern Mediterranean (4.6%) and western pacific (3.9%)[1]. It may be associated with liver cirrhosis in 5-20% of patients over a period of 20-25 years and 30% of them may develop end stage liver failure over a period of 10 years[4]. Of those with cirrhosis 30-50% may develop Hepatocellular carcinoma[2]. Other extra hepatic complications are mixed cryoglobulinaemia, non-Hodgkin lymphoma and membrano-prolifeartive glomerulonephritis[2,4]. Due to these serious complications, it becomes essential to treat the infected patients. If a sustained virological response (SVR) can be achieved with treatment, all the complications may be prevented and natural history of the disease may change[2]. Previously it was known as Non A, Non B hepatitis. In 1989 it was named as Hepatitis C virus[5,6]. Response to interferon alone was not very encouraging but combination therapy with interferon and ribavirin for 48 weeks increased the response rate significantly to 63-66% compared to 7-11% with interferon monotherapy[7,8,9,10,11]. Response rate improved further after the introduction of pegylated (peg) interferon. In Asians, improvement was better than Caucasians[2,12].

Treatment response depends on various variables including genotype, pre and post treatment viral load, serum ALT level, platelet count, body mass index (BMI), co infection with Hepatitis B, alcohol consumption and duration of therapy[4,13,14]. Current standard treatment of chronic hepatitis C is either standard interferon α 2a or 2b (3 million international units (MIU) subcutaneously (SC) three times weekly) or Peg-interferon along with ribavirin[15]. Peg interferon

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and ribavirin are more effective for genotype 1. But the results for genotype 2 and 3 with both types of interferon are almost similar so that for these genotypes standard interferon can be used instead of peg interferon[11]. It is a great advantage because former is much cheaper than the later. In developing countries like Pakistan, standard interferon α with ribavirin is still the mainstay of treatment especially in government funded treatment programmes for hepatitis B and C.

In Pakistan prevalence of Hep C is more than 3% and genotype 3a is more prevalent followed by 3b, 1a, 1b and 2a; type 4 is least common[3]. Success of treatment is usually judged by measuring viral load. If it is undetectable by a sensitive laboratory test i.e. PCR (Polymerase chain reaction) at the end of treatment and six months after completion of therapy, it is termed as end of treatment response (ETR) and sustained virological response (SVR) respectively[4]. Goal of treatment is to eradicate the infection which is considered to be achieved if a patient gets SVR[1,4]. For genotypes 2 and 3, treatment for 24 weeks is usually sufficient[1].

We have tried to determine the response rate to standard interferon α and ribavirin in our patients infected with genotypes 2 and 3. Response rate of this regimen can vary in different populations as is shown by the different response rates observed in local American whites and blacks[4]. This may be attributed to differences in the natural immunity against the infection. We wanted to observe the situation in the area under study and compare it with the results in other parts of the world. This may also be useful to rationalize the treatment of genotype 2 and 3 with standard interferon and ribavirin, a much cheaper option than peg interferon.

We also wanted to determine the tolerance of the patients to this regimen by studying its side effect profile and dropout rate from the treatment program.

MATERIALS AND METHODS

This was an observational study conducted at Saleem Medical Complex and Maryam Maternity home, Kotli, Azad Kashmir, from January 2012 to December 2012. It included a total of 150 patients of chronic hepatitis C, both males and females, aged 20 years and above. Those who had already received interferon and ribavirin therapy were not included. In patients of chronic hepatitis C, who were diagnosed with ELISA (Biocheck USA), both the quantitative and real time qualitative PCR were done on Rotor-Gene g6000 by using Qiagen Artus (Germany). In those with positive PCR results, genotyping was done by Ohno Multiplex PCR method. Only patients with genotype 2 and 3 were included in the study. Liver biopsy was not done. In patients included in the study, liver function tests, urea, creatinine, prothrombin time, serum albumin, blood sugar, full blood counts along with platelet counts and abdominal ultrasound were performed. Patients with decompensated cirrhosis, very low TLC (<2500/ml) and platelets (<140,000 /ml) were excluded from the study. Informed consent was taken from the patients before starting them on treatment. They were given interferon alpha-2A, 3 MIU subcutaneously on alternate days and Ribavirin in a fixed dose of 400mg twice daily. Treatment was continued for 24 weeks. Patients took oral treatment at home and injection interferon at health facility near their homes. They visited Saleem Medical complex initially fortnightly and later on monthly for their clinical assessment, complete blood picture, ALT and abdominal ultrasound. All the information was recorded and side effect profile was maintained. At the completion of therapy, PCR was done to detect ETR and again six months later after completion of therapy to document SVR. Data was analysed by simple mathematics calculating percentages and using Excel 2013.

RESULTS

Among a total of 150 patients, 30 (20%) were males and 120 (80%) were females. Most of the patients were between 20-49 years of age (83.99%) (Table 1). ETR was 82% (n=123) and overall SVR was found to be 65.33% (n=98). (Table 2) Out of 123 with ETR, 25 (20.33%) patients relapsed. From a total of 150 patients, 52(34.67%) could not achieve SVR (27 non-responders and 25 relapsed). (Table 2)

Table No.1: Age wise distribution of patients who were given treatment for hepatitis C

Age group (years)	Number of patients	percentage
20-29	38	25.33%
30-39	40	26.66%
40-49	48	32%
50-59	15	10%
60-69	8	5.33%
70 and above	1	0.66%
Total	150	100%

Table No.2: Frequency of patients with ETR and SVR

	Patients with positive response		Non responders/ relapsed		Total number
	Numbers	%age	Number	%age	
End of treatment response (ETR)	123	82	27	18	Total patients 150 (100%)
Sustained virological response (SVR) out of ETR	98	79.67	25	20.33	Total with ETR 123 (100%)
Overall SVR	98	65.33	52	34.67	150 (100%)

Fever was the most common adverse effect observed during therapy (50%; n=75). Flu like symptoms, headache and hair loss were other common treatment

related adverse effects (26.66%, 20% and 13.33% respectively). Anaemia and thrombocytopenia were observed in 10% subjects each (n=15 each) but they were not severe enough to warrant for the discontinuation of therapy. Rates of neuropsychiatric problems (depression and encephalopathy) were low. (Figure 1) There was no death and all the patients completed the treatment.

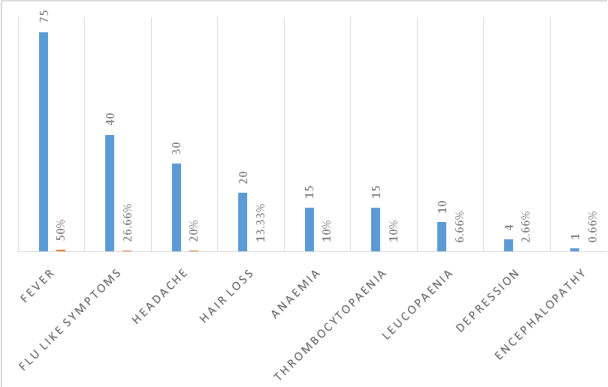

Figure No.1. Frequency of complications in patients receiving treatment for hepatitis C with standard interferon and ribavirin

Digits on top of the bars show the numbers and on side, the percentages

DISCUSSION

Treatment of Hepatitis C is important to prevent the morbidity and mortality and to control its spread in the community. From the earlier studies it was apparent that response rate to treatment was much higher for genotypes 2 and 3 as compared to genotype 1[16]. It was also documented through various studies that combination therapy with interferon and ribavirin was more effective and both new and relapsed cases gave better results with combination treatment than interferon alone[9,17]. In our study, ETR was 82% and SVR was 65.33%. This was quite an encouraging result, indicating a good response rate in the study population. In patients who develop SVR, natural history of the disease is altered and further progression either reverses or slows down with resultant decrease in complication rate[2]. An early viral response (EVR) (at least 2 log decrease in viral load by the end of 12 weeks of therapy) is a good predictor of SVR[11,13,17]. Rapid response at week 4 predicts achievement of SVR[18]. A viral load of <400,000 at the beginning of therapy was associated with good EVR[13].

Low platelet count (less than 140,000/ml) and high BMI (>30) are associated with relapse rate of 27.5%[4,13]. Poynard et al has included "age less than 40 years" and "female gender" as good prognostic indicators[10]. Alfredo Alberti mentioned that age alone could predict the disease outcome due to the presence of other metabolic co factors[19]. With increasing age, the chances of other co morbid conditions are higher while the chances of adherence to treatment are low[20]. Low albumin (less than 4 gram/dL) can also be taken as poor outcome predictor[21]. Presence of IL28BSNP (Interleukin 28B Single Nucleotide polymorphism) genotype confers a higher chance of achieving rapid virological response (RVR)[13,22]. Co infection with HIV, Hepatitis B and alcohol use further accelerate the chronic complications of hepatitis C[23].

In our study 27 (18%) were non responders. What should be the strategy for those who fail optimal treatment with interferon alpha and ribavirin is difficult to decide. They may be started on peg interferon and ribavirin but response rate is low (10%)[4]. Early disappearance of virus is associated with higher chances of achieving SVR. If there is low RVR and EVR, it is prudent to make early decisions about the continuation of treatment[7]. According to a study, 99% of those who attained SVR, maintained long term viral clearance for more than six year[24].

Patients in our study tolerated the therapy well and all of them remained adherent to the treatment till the end. A Japanese study showed that withdrawal rate from treatment was 13% in patients more than 65 and 7% in less than 65 years of age[25]. Interferon and ribavirin can lead to many haematological adverse effects[25,26,27].

CONCLUSION

Our study showed that response rate of patients with chronic hepatitis C, genotype 2 and 3, to standard interferon alpha and fixed low dose ribavirin was good. Side effect profile was favourable with minimum of adverse effects which did not lead to discontinuation of treatment. So conventional interferon which is cheaper, may be used instead of peg interferon in infection with genotypes 2 and 3. For non-responders and relapsed patients it is important to look for new, effective and cheap treatment options that are easily affordable by the poor local population.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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ACKNOWLEDGMENTS

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