Med. Forum, Vol. 22, No.4 April, 2011 **ISSN 1029-385-X**

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Editorial

Violence against women is a public health problem

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Like civilian bureaucracies, militaries, corporations, banks and financial institutions and even many universities and centers of research all over the world, the UN too has largely been a 'boys club for all the 62 years of its life. It's a civilized way of chalking up the global hierarchy and pecking order. However, probably because the UN is ageing and still hasn't produced the successes expected from the men, it is now allowing women to take charge of their own lives.

To date, nothing essentially has changed in the world unless the head honchos represented in the Security Council said so. The exception would be when too many innocents are killed, maimed, ruined or enslaved by war and the destruction as well as the loss of lives becomes difficult to cover up. It is under these circumstances that many member-countries including the 'advanced' North demand a stop, forcing aggressors to pull back or lighten their touch to avoid looking too much like a rogue state. Also the UN doesn't want to completely lose its moral credibility.

The UN is a massive organization, with all the slowness, red-tape and waste that accompanies huge bureaucracies, perhaps the world's biggest since it is represented in multiple ways in most countries - 20 specialized agencies plus 8 expert bodies; 17 functional, regional and standing committees under the Economic and Social Council; and 11 subsidiary bodies under the Security Council including the Working Group on Children and Armed Conflict, which doesn't seem to have helped much. But judging from the state of the world, it is largely ineffective, partly because it didn't have enough women or the right ones in the right places.

However, over the decades, the UN has tried to compensate for its glaring core inequalities by doing its bit for women and children through UNFPA. UNICEF and WHO as well as ILO. The 1LO and FAO which were expected to do much more for female labour but the urban and rural problem with both the organizations, however, is that the former does not pack enough of a punch; while the latter, despite earlier good research work, shockingly aligned itself in recent decades with corporate interests in agriculture. That sounded a death knell for healthy food, the environment and the livelihoods of women peasants practicing small-scale, organic indigenous farming.

The UN tried to improve itself by turning to other tracks as well but mostly in vain. There was the Beijing Conference on Women 15 years ago. Then Beijing+10 (years) to remind governments of their unfulfilled promises. And recently, Beijing+15, but it was already clear that the Beijing route wasn't going to get anywhere. The UN also tried the Millennium Development Goals or MDG to persuade or shame governments into doing what was their taxpayer-paid job to do anyway - like seeing to female health care, education, basic rights, etc. But shame is an alien concept in the upper echelons of many governments, our own being a prime example. MDGs proved even less interesting, although lip-service was paid to them: and even rendered impossible, since the UN's rogue siblings, the World Bank and IMF, had drowned most of the South in debt.

One of the UN's biggest failures is its distance from the media. Excellent and in-depth research by various agencies and their programmes are not publicized: and if they are, the approach is too weak to grab media interest. In fact, a number of UN's humanitarian or more humane agencies could have done much better if they were less academic and more activist. In hindsight it would appear that some of these organizations were deliberately tied up in knots through restrictive mandates to keep them in line.

The action towards UN WOMEN began when some major national, international and regional women's, human rights and social justice organizations in various countries and regions became dissatisfied with the UN rhetoric not matching promises for gender equality. They began to lobby and pressurize for a meaningful outcome through a specialized agency focusing exclusively on women. It turned into the Gender Equality Architecture Reform or GEAR Campaign, a network of over 300 groups around the world launched on the 7th of June this year. Pakistani women activists were also in the action.

On 2nd July, the UN General Assembly voted unanimously to create the new women's entity, to be known as UN WOMEN. The new head (yet to be appointed) would be a woman Under-Secretary General, second only to the Secretary General. It should have made headlines in the global media, but it didn't. Was it because, as many women point out, that the media in great part if not in entirely, especially the corporate media, is also male-biased? Or was it yet another routine UN failure with the media? Most likely, both.

Earlier, the UN had some exclusive offices for women, too small, scattered and under-resourced to be effective. The Division for Advancement of Women (DAW), the UN International Research and Training Institute for the Advancement of Women (INSTRAW), Office of the Special Advisor for Gender Issues (OSAGI), and UNIFEM (UN Development Fund for Women) which was the largest of the four and chronically short on funds. But none of them, not even UNIFEM, had access to the decision-makers at the highest level, rendering them into nothing more than tokens. Now all of these offices will be amalgamated into one. while adding on others.

There's feverish lobbying for the slot of Under-Secretary General, as almost every continent wants to be represented, although it would not do if the appointee is not from the South. The women's lobby sought a billion dollars; the Secretary-General said half-a-billion for starters, suggesting that it takes off in the 80 countries where UNIFEM is already present. After all, UN salaries and New York costs are high, and gender equality requires the women to be on the same level as men.

So why is UN WOMEN based in New York when it should be more appropriately installed in a third world region where the bulk of the problems and injustices occur? That only the men can answer, or probably will not answer, because certain countries or at least one hegemonic country would like to keep it on a tight leash so that it doesn't get too big for its heels.

UN WOMEN is going to have, not a full plate, but an overflowing one. Most other UN agencies are specialized, but have not succeeded in maintaining gender parity. UN WOMEN will have to look at all those areas and more. Not just gender equality among the educated middle-class and elite, and not just for the governments and parliaments, but also for the unrepresented majority, the ordinary women of the world - peasants, home-makers, factory, clerical, domestic and service workers alike - who outnumber their better-off sisters 6 to I, and who have been invisible for and in the UN throughout.

UN WOMEN will have to take on environmental issues in a way that UNEP, the UN environmental agency, has never been able to solve: that includes land and water issues on which women's livelihoods depend as they are the ones who produce and provide food for most families. It will also have to take on the multinational corporations and foreign investors that continue to ruthlessly exploit and poison the world, particularly the oil, agro-based industries, and pharmaceutical companies.

UN WOMEN will have to make itself more inclusive so that non-academics and unlettered women, who have achieved much for their fellow-women, can participate and share their expertise directly instead of through jargonized documentation by people who never go into the field or sweat.

UN WOMEN has to be accessible in a way that the UN has never been for ordinary people, especially women, as it is no longer enough to hide behind the excuse that it represents governments only, especially when they fail. Too many governments are unrepresentative of the people including some hegemonic powers, and too many are corrupted by some wealthy governments and multinational corporations as well as the unaccountable, non-transparent World Bank and IMF. But women have always found ways around and have endured much. Hopefully these circumstances will change as more women come into power and are handed over the authority to make a difference.

Original Article

Oesophageal Atresia - Experience of 7 Years with Data Evaluation

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ABSTRACT

Objective: Study conducted for evaluation of Oesophageal atresia patients to assess the factors influencing the survival and outcome.

Design of Study: Prospective analytical study.

Place & Duration of Study: This study was conducted in dept. of Paediatric surgery at peoples medical college, Nawabshah. from September 2001 to September 2008.

Patients and Methods: A prospective analysis of 37 cases of Oesophageal Atresia (EA) was performed. In this study, 37 neonates were admitted with the diagnosis of EA with or without TEF .The data were collected retrospectively from hospital charts. The preoperative assessment of upper pouch was done with plain X-ray chest with 8 Fr Red Rubber catheter. The associated congenital anomalies were evaluated on the basis of careful examination, radiological and sonological investigations.

Results: The commonest type of Oesophageal Atresia was with distal Tracheoesophageal Fistula (TEF) in 32 cases (86.48 %). Associated anomalies were present in 50% patients, cardiac was commonest followed by gastrointestinal anomalies. Vacterl association was found in 6 (16.21 %) cases. Prematurity, associated congenital anomalies, gap between esophageal ends and preoperative respiratory status were the significant factors affecting the survival. Primary extra pleural repair was the surgical approach in most of the patients except two with difficulty that change to intra pleural approach. Retro pleural drainage was used in 32 classical type 1 cases. Staged procedures were performed in 5 cases of isolated Oesophageal Atresia. Pneumonitis and sepsis were the most common early postoperative complications (30%). Sepsis and cardio respiratory arrest were the most common causes of mortality 11 cases (18.91). Oesophageal leak found in 3 cases, including 2 major and 1 minor leaks. Major leak followed by sepsis caused 1 Deaths. Survival as per Waterston criteria was 85% in group A, 66.6% in group B and 20% in group C.

Conclusion: Factors affecting the survival of patients with Oesophageal Atresia are major or life-threatening associated anomalies, long gap, pneumonia and sepsis at presentation or that acquired during hospitalization and major leaks. The high incidence of low birth weight, delayed diagnosis, poor referral, low-socio economic status and lack of advanced neonatological back up are important contributory factors to poor outcome.

Key Words: Oesophageal Atresia (EA), Tracheoesophageal Fistula (TEF), Pneumonitis and sepsis

INTRODUCTION

The survival of infants born with esophageal atresia (EA), tracheoesophageal fistula (TEF), or both has improved dramatically since Cameron Haight's first successful repair in 1941[1]. Improvements in survival are largely attributable to refinements in neonatal intensive care, anesthetic management, ventilatory support, and surgical techniques. Survival may now be achieved in infants with low birth weight[2], with mortality limited to those patients who have severe life-threatening anomalies

Because of innovative modalities nowadays there has been improvement in management and mortality been reduced coupled with improved anesthesia and good neonatal care. At present, in most of the developed countries, only the presence of associated major congenital anomalies determines the chances of survival[3]. This is not the same in developing countries, where many other preoperative, postoperative and socioeconomic factors continue to contribute to the persisting high mortality. [4],[]In our study we have seen only those factors which has significant importance in the survival rate.

PATIENTS AND METHODS

In this study, 37 neonates were admitted with the diagnosis of EA with or without TEF .The data were collected retrospectively from hospital charts. The preoperative assessment of upper pouch was done with plain X-ray chest with 8 Fr Red Rubber catheter. The associated congenital anomalies were evaluated on the basis of careful examination, radiological and sonological investigations.

Infants were also assigned to risk groups A, B, or C as described by Waterston and associates[6]

- Group A
- 1. Birth weight >2,500 g and well
- Group B
- 1. Birth weight 1,800 to 2,500 g and well, or
- 2. Birth weight >2,500 g but moderate pneumonia and other congenital anomaly
- Group C
- 1. Birth weight <1,800 g or
- 2. Birth weight >1,800 g with severe anomaly or pneumonia

Data collected included age at the time of admission, gestational age, birth weight, sex, site of delivery, history of feeding, associated congenital anomalies, respiratory status, presence of pneumonitis, type of anomaly, operative technique, gap (measurement done intraoperatively), complications and esophageal anastomotic leak and their impact on survival. Waterston prognostic criteria were used for survival.

All the patients operated retropleurally with classical steps ligation of fistula and end to end anastomosis of esophagus and per esophageal drainage along with stent placed. Esophageal anastomosis was performed by 5-0-vicryl single layer interrupted sutures. Feeding started after 48 h of surgery and gradually increased. Because of presence of stent. Contrast esophagogram was done on the sixth day of surgery. Anastomotic leaks after the primary repair were detected either by observing the saliva in the retro pleural drain or by contrast esophagogram. Minor leaks were identified by appearance of frothy saliva in the retro pleural drain with no accompanying deterioration in the general condition. Major leaks were clinically suspected by the contents draining with the accompanying deterioration in the general condition of the patient either due to mediastinitis and septicemia. The finding of contrast in stomach without any clinical deterioration was considered normal.

The term minor leak was used for a small amount of extra pleural leakage and/or a small radiological leak and major leak referred to a large amount of drainage or a leak that caused respiratory symptoms associated with a large defect in anastomosis

RESULTS

Esophageal atresia with distal TEF was the commonest type present in 32(86.48 %) cases; .isolated esophageal atersia without fistula found in 5. Associated congenital anomalies were present in 18 (49.54%) patients, including cardiac diseases in 17 patients, gastrointestinal in 7 cases, vertebral and nervous system anomalies in 8 cases, musculoskeletal anomalies in 4 cases, head and neck problems in 1 cases, genitourinary anomalies in 2 cases and respiratory system anomalies in 2 cases with cleft lip in 1 case. Vacterl association was present in 5 (13.51 %) cases.

Preoperative details and their impact on survival are given in Table 1.

Table 1: Pre. Operative Details With Survival

		Total Cases %	Survival %
Age	< 24 hrs	09 (24.3)	05 (13.5)
	24-48 hrs	13 (35.1)	07 (18.9)
	> 48 hrs	15 (40.5)	14 (37.8)
Maturity	Full Term	27 (72.9)	22 (59.4)
	Pre Term	10 (27.7)	04 (10.8)
Weight	>2.5 kg	20 (54.0)	13 (35.1)
	1.8-2.5 kg	14 (37.8)	10 (27.0)
	< 1.8 kg	03 (8.10)	03 (8.1)
Sex	Male	20 (54.0)	17(45.9)
	Female	17 (45.9)	09(24.3)
Place of Delivery	Home	16 (43.2)	09 (24.3)
	Hospital	21 (56.7)	17 (45.4)
Feeding History	Present	24 (64.8)	20 (54.0)
	Absent	13 (35.1)	06 (16.2)

Only 8(21.62 %) were having no respiratory distress at the time of admission; 12 (32.43 %) were having mild, 8 (21.62 %) were having moderate and 12 (32.43 %) were having severe respiratory distress. Clinically and/or radiologically chest was normal only in 8 (21.62 %) cases, with mild pneumonitis in 8 (21.62 %), moderate pneumonitis in 5 (13.51 %) and severe pneumonitis in 5 (13.51 %) cases. Short gap (<1 cm or one vertebral body) was found in 15 cases (40.54 %), intermediate gap (1-3 cm or 1-3 vertebral bodies) in 12 (32.43 %) and long gap (>3 cm or 3 vertebral bodies) in 5 (13.51 %) cases. Survival rates were 89%, 60% and 23% in cases of mild, moderate and severe respiratory distress, respectively. Survival was 82% in patients with no preoperative pneumonitis falling down to 75%, 72% and 23% with mild pneumonitis, moderate pneumonitis and severe pneumonitis, respectively. Gap was a highly significant factor affecting the survival with 91% survival in short gap and dropping down to 69% and 53% in the intermediate gap and long gap, respectively.

Table 2: Survival according to Waterston

Waterston Classification	Total Cases	Survival
A	20 (54.05%)	17 (85%)
B	12 (32.43%)	08 (66.66)
C	05 (13.51%)	01 (20%)

Our primary approach in all the patients of EA with TEF was extra pleural; however, in 2 cases of EA with

TEF, extra pleural approach was converted to transpleural because of the severe inflammation of parietal pleura in patients with severe pneumonitis or inadvertent breeches in the pleura during the surgery. In the primary repair of EA, azygos vein was ligated in all cases and retro pleural drainage was not performed in 32 cases. Transanastomotic stenting for early feeding after 24 h of surgery was carried out in all 32 (86.4 %) cases.

Table 3: Survival According To Procedure

	Primary Procedure	Survived	Staged Procedure	Survived
Oesophageal atresia with TEF	32	22		
Isolated OA			05	4

Staged procedures were done in 5 cases of EA still under follow-up as given in Table 3

All 4 among 5 cases of isolated esophageal atresia surviving cases are in follow-ups waiting for esophageal replacement.

Out of 32 cases of EA, 10 patients faced early postoperative complications; commonest complication was sepsis with pneumonitis, followed by sepsis alone. The commonest cause for mortality in cases with early postoperative complications was cardio respiratory arrest secondary to hypoxia and pneumonitis in 7 cases. Delayed postoperative complications such as pneumonitis, sepsis, major anastomotic leak, aspiration and tracheomalacia were present in 8 (25%) cases that were responsible for mortality in 3 cases. Major anastomotic leak in patients of EA after primary repair was seen in 2/31 (5.40 %).

DISCUSSION

We have observed few important things to improve outcome in esophageal atresia patients .most of the patient presented late in our territory because of non availability of concerned surgeon nearby so age is bad prognostic marker in our study . Although none of the previous studies from abroad has considered age as a probable risk factor. Prematurity is still a major problem for developing countries due to the additional physiological handicaps in these babies and the increased susceptibility to sepsis. [7

Weight at the time of presentation again a high risk factor and less than 1.8 kg weight has bad prognosis Spitz *et al.* [8] . place of delivery affects the survival as in our study because or referral from rural areas so sepsis is pronounced in such cases as compared to study conducted in developed countries where deliveries conducted in hospitals. Fewer number of female patients is because of male dominant society in our coutries and not presenting female babies .Our findings are similar to that of Bindi *et al* . [9]

Associated anomalies are not so different from those of Hassab *et al.* [10] who reported 60% associated anomalies with VACTERL association in 6%. Spitz *et al.* [8] reported 47%, Saing *et al.* [11] reported 59% and Rokitansky *et al.* [12] reported 52.4% associated congenital anomalies. The survival rate among these cases was low (43%) as compared with 78% in those free from any other congenital anomaly. This shows that association of other congenital anomalies plays a major role in the survival of patients with EA ($P < 0.001$). The survival rate among the patients with EA with congenital heart disease (CHD) was 33% ($P < 0.001$), while in the series of Ein *et al.* , [13] 64% of the neonates of EA with CHD survived. Similar findings had been reported by Choudhury *et al* . [14] The presence of long gap is significantly associated with the poor survival rate ($P < 0.001$). This is because the long gap is associated with high incidence of anastomotic complication and other congenital malformations. Brown *et al.* [16] and Sharma *et al.* , [17] in their study of the measurement of the gap length and mortality in EA, also reached the same conclusions.

The history of feeding that is present in several patients in our study is because of illiteracy and a tradition of giving ghutee after the birth of a neonate, The survival rate was statistically not significant; the reason may be that the neonates who were fed did not have life-threatening anomalies.. Feeding through naso gastric tube makes no significant difference in survival. Kevin *et al,* [18] but we have seen early feeding in stable patients make early recovery. Peri Anastomotic drain placed all patients with classical type esophageal atresia which is veri necessary in all cases as early recognition of complications but Gangopadhyay *et al.* [19] recommended that retro pleural drainage is not necessary in all the cases of EA.

In our study, 32/37 (86.48 %) patients of EA with TEF had primary repair in which

25 (67.56%) patients survived as compared with 36% survival rate in the series of gangopadhayay et al [19] .

In isolated esophageal atresia 5 cases staged procedures (cervical esophagostomy and abdominal esophagostomy or cervical esophagostomy and ligation of the distal esophageal end with gastrostomy) done. Bhatnagar *et al* . [20]studied the exteriorization of the distal esophagus in the abdomen in EA patients with indications of long-gap atresia or isolated esophageal atresia without TEF.

Out of 32 cases of EA, 10 faced early postoperative complications that were responsible for mortality in 7 cases. The most common complication was sepsis , however, the most common cause for mortality was cardio respiratory arrest

Most of these early postoperative complications are not related with surgical procedures. Delayed postoperative complications such as pneumonitis, sepsis, major

anastomotic leak, aspiration and tracheomalacia were present in 8 (15.62 %) cases, and these complications were responsible for mortality in 4 cases. Factors predicting mortality were pneumonia and sepsis at presentation or that acquired during hospitalization, major or life-threatening anomalies, long gaps and major leaks. Similar postoperative complications are also reported by Bindi *et al.* [9] and Hassab *et al.* [10] The incidence of anastomotic leak in patients of EA after primary repair was observed in 3 patients with major leak in 2 (6.25 %) and minor leak in 1 (3.12 %) patients. Spitz *et al.* [8]and McKinnon and Kosloske *et al.* [21] also reported anastomotic leak in 21% cases. Amongst patients with major leak, seven patients associated with pneumonitis or septicemia expired. On comparing the survival rate among patients with major leak and patients without major leak the difference was found to be statistically significant . Statistically significant difference was observed between the survival rates among different classes of Waterston. Spitz *et al.* [8]had earlier reported that survival rates according to Waterston classification was 100% for class A, 86% for class B and 73% for class C cases. In the series of Bhatnagar *et al.* , [7] the survival was maximum in group A (67.6%) and it dropped down to 28.8% in group C. At present, the survival rate has improved in Group A and B; however, it has remained almost the same in group C. On comparing the data of the present series with that of Hassab *et al.*, [10] it was established that although the distribution of cases as per Waterston classification in both these setups were different, the survival rates were almost similar. Our results for survival in class C are lower as compared with other studies, for which the reason might be the higher incidence of low birth weight, delayed diagnosis, poor unsupervised transport, low socioeconomic status and lack of advanced neonatological back up. Waterston classification was statistically the best application in our study. We also propose that the survival in EA can be used as an index for the status of neonatal surgical care because EA had the highest mortality rate amongst all the surgical conditions because of the problems in respiratory care and surgical technical failure. [22]

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Original Article

Serum Magnesium and Hypertension

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ABSTRACT

Background: Despite advances in the prevention and treatment of hypertension over the past decade, hypertension remains an important public health challenge. Recent efforts to reduce the prevalence of hypertension have been focused on non-pharmacologic means, specifically diet. An increased in take of magnesium has been shown in some but not all studies to reduce blood pressure in patients with hypertension. Decreased Serum magnesium levels are associated with development of hypertension.

Aim: This study was planned to investigate relation of serum magnesium with blood pressure in patients with mild uncomplicated hypertension.

Place and Duration of Study: Study was conducted at LUMHS hospital Jamshoro and DHQ hospital charssadda for the period of six months.

Patients & Methods: Fifty known cases of uncomplicated mild hypertensive patients were selected, same number of healthy controls were also examined.

Results: When results were summed up and test parameters were compared, it was seen that no significant differences were found in serum magnesium levels among both groups, when compared statistically.

Conclusion: Finally we conclude that no relation of magnesium with hypertension was observed.

Suggestions: Much more work on wide scale population may be needed to clarify the idea.

Key Words: Magnesium, Hypertension, Ischaemic heart disease (IHD), Diabetes.

INTRODUCTION

Ischaemic heart disease (IHD) is a leading cause of death in most of industrial and western world. A number of risk factors are associated with IHD. Major being: hyperchlesterolaemia, hypertension, cigarette smoking, diabetes mellitus and stress and strain. Hypertension is an important accelerator of the atherosclerotic process and it frequently accompanies adult ischaemic heart disease[1]. Hypertension is associated with an increased risk of clinical cardiovascular complication due to atherosclerosis and atheroma develops earlier in these patients. There are significant differences between the severity of the lesions of atherosclerosis in hypertensive and non-hypertensive subject [2]. Magnesium is a biologically essential cat ion, has recently received considerable attention in clinic medicine, especially with regard to the role of its depletion in cardiovascular pathophysiology [3]. Magnesium is the fourth most abundant cat ion in the body and the second most abundant intra cellular cat ion, next to potassium [4]. Some authors have shown recently an increasing interest in the effects of calcium and magnesium on blood pressure [5]. Many reports have appeared in recent year discussing association between serum magnesium levels and Hypertension. Accumulating evidence implicates a role of magnesium and pathophysiology of essential hypertension [14, 15] but its role in pathophysiology is still unclear [16]. Present study was carried out to this burning issue. Study was aimed to investigate this relation.

PATIENTS AND METHODS

Study was conducted in the department of cardiovascular diseases, LUMHS, Jamshoro and DHQ teaching Hospital, Charsadda, for the period of six months. Fifty known cases of mild uncomplicated hypertension were selected. Same numbers of healthy control were also selected. The information about name, age, sex, duration of their illness and blood pressure, smoking habits, and family history of cardiovascular disease were recorded. Patients with diuretic therapy, thyroid abnormalities, liver failure, renal failure or alcoholics were excluded form the study. Fifty healthy controls were selected with no preexisting cardiovascular disease. A single casual supine blood pressure measurement was obtained by trained staff using a standard mercury sphygmomanometer according to W.H.O criteria. Blood samples of patients and healthy controls were drawn from antecubital vein by taking aseptic measures for determination of serum magnesium levels. Statistical analysis was done by student's t-test.

RESULT

When results were summed up and test parameters were compared it was seen that mean age of patients and controls was 40-50 years ± 0.1 Serum magnesium levels (table) in control subjects were 2.94 ± 0.05 mg/dl, while mean serum magnesium levels in hypertensive subjects were 2.89 ± 0.03 mg/dl. The differences were found-non-significant (p>0.5) when evaluated statistically.

Table: Comparison of mean values serum magnesium (mg/dl) in controls and hypertensive patients.

Group	Blood Pressure (mmHg) Systolic/diastolic		Serum magnesium (mg/dl)	P-value
Controls (n=50)	126.00 ±_1.87	79.96 ±_1.39	2.94 ±_0.05	>0.5
Patients (n=50)	155.00 ±_1.52	103.62 ±_1.21	2.83 ±_0.10	>0.5

Each value represents mean of individual observation ± indicates standard error of mean.

DISCUSSION

Investigations of the association between serum magnesium and blood pressure have yielded conflicting results. Hvarfner et al. found a positive association between serum magnesium and blood pressure in 58 hypertensive patients and 124 controls studied in Uppsala, Sweden. There was no difference between the relation identified in the hypertensive and control groups [7]. The relation between serum magnesium and blood pressure has also been examined by using data from national health and nutrition (NH&N) survey, no association was identified between serum magnesium and systolic blood pressure [8]. Similarly, data from a community based cross sectional study of elderly whites in Baltimore provided no evidence of an association between serum magnesium and blood pressure [9]. Peterson and co-workers reported a significant increase in correlation between serum magnesium levels and systolic blood pressure [10]. Rinner et al studied Dutch population, and they found no relation between serum magnesium and blood pressure[11]. Altura and Altura have reviewed the mechanism underlying in the relationship between magnesium and blood pressure. It has been postulated that if the concentration of extracellular magnesium is lowered, calcium infux is enhanced. There is relatively little information form both animal and human studies to indicate direct relationship between magnesium and blood pressure [12]. Similarly, Herzog in 1995 also failed to establish any relationship between blood pressure and serum magnesium [13]. In the present study, it was observed that the serum magnesium levels in patients with hypertension and in controls are with in normal limits. Therefore our study suggests no relation between serum magnesium levels and blood pressure in the patients of hypertension. Therefore, this study is in the favor of works done by whelton et al. Rinner et al. Cappuccio et al. And Herzog et al [6, 9, 11, 13] Our results are in contrasts with the study done by Hvarfner et al. as they found high serum magnesium levels in hypertensive patients [7]. Also, study of peteson and co-workers reported decreased levels of serum magnesium in hypertensive patients, conflicts with our study [10]. Finally we suggest that further large scale studies on a large population are to be carried out to clarify idea.

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Original Article

A Survey to Assess the Female Sexual Harassment in the Higher Educational Institutes of Karachi

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ABSTRACT

Objectives: To determine the nature and frequency of the exposure of female students to sexual harassment at higher educational institutes; and explore the adverse effects of sexual harassment on the victims and coping strategies implied by them.

Background: Sexual harassment, whether at workplace, educational institution, street or leisure is a problem gaining increasing recognition in every society. Despite the widespread nature of the problem, there are still considerable misunderstandings as well as differences of opinion concerning whether particular situations or behaviours are sexually harassing in nature or not. The victim may feel threatened, humiliated, harassed, and would interfere with the performance, satisfaction, commitment, and undermine security, or create an intimidating environment.

Place and Duration of Study: This study was conducted in ten institutes which included six medical, three engineering and one general colleges/universities of Karachi from January 6 to September 30, 2009.

Patients and Methods: A total 480 female students were conveniently selected from ten different educational institutes, and were provided a self administered questionnaire with their consent. The identity of all the study subjects was kept secret.

Results: Out of total 480 female students, 460 i.e. 96% returned the filled questionnaires. Among them, 65% reported of sexual harassment of various degrees / levels irrespective of their residential area, appearance and attire. These females were harassed by the fellow students (37%), faculty (32%), and strangers (64%) who included patients, attendants, visitors and passersby. Although almost all of the participants (98%) wanted a punishment for the harassers, yet they (78%) were reluctant to disclose the name / identity of those perpetrators because of the fear of exploitation, social taboo, further embarrassment, adverse consequences, and career obstacles.

Conclusion: Many females were the victim of sexual harassment in various forms. There is a need to sensitize the society; and mass awareness programs should be carried out through variety of media.

Key Words: Sexual harassment, females, gender discrimination, educational institutes.

INTRODUCTION

The review of the relevant literature suggests that sexual harassment is a very serious social and psychological issue and the women from every walk of life are affected by it.[1,2] Perceptions differ about what behaviors constitute sexual harassment. However, typical examples of sexual harassment include sexually oriented staring, verbal harassment or abuse, subtle pressure for sexual activity, sexist remarks about a woman's clothing, body, or sexual activities, unnecessary touching, patting, or pinching, leering of a woman's body, use of pornographic material, grabbing, non-reciprocated requests for dates; intrusive letters and phone calls, gross sexual imposition or assault accompanied by implied or overt bribes or threats concerning one's job, grades, letters of recommendations; and rape, etc.[3]

Sexual harassment in education remains a "forgotten secret," with educators and administrators refusing to admit that the problem exists in their institutes, or accept their legal and ethical responsibilities to deal with it. The harassers are usually men, while victims or targets are usually women. This pattern reflects prevalent social power relations.[4]

Sexual harassment is a reality at school, and in the work place,[5] has consequences for psychological ill-health among adult women;[6] and the young girls who reported being sexually assaulted or harassed often tend to develop emotional disorder and exhibit suicidal behavior more frequently.[7]

Sexual harassment is so widespread that we often fail to recognize the harassing behavior as wrong. This is because so many of us (women and men alike) have become desensitized to offensive behaviors.

The cases of sexual harassment are not reported by victims because of various reasons such as family and peer pressures, unsatisfactory police behavior, the long and unjust processes in application of law and lack

of insecurity on the part of the victim. Sexual harassment is the least spoken issue in Pakistani society. Although all women know it and experience it but nobody cared or dared to report it because throughout their lives they had been discouraged to speak about such incidences.[8]

This survey was conducted to determine the exposure of female students to sexual harassment, and coping strategies implied by them.

PATIENTS AND METHODS

This study was conducted in ten institutes which included six medical, three engineering and one general colleges/universities of Karachi. Around 800 female students were contacted in these institutes and were explained the purpose of the study, but 480 of them volunteered to participate and the rest refused to talk about this social taboo. This also has been earlier reported that sexual harassment was difficult to study as it was the least spoken issue in Pakistani society.[8] After taking a verbal informed consent, a pre-tested questionnaire was distributed amongst study participants. A convenient sampling technique was adopted and the study subjects were approached in the girls' common rooms, libraries, class rooms, laboratories, canteens and corridors of these institutes. They were assured of the secrecy of their identity and their names were not mentioned in the proforma. The data was analyzed by using SPSS Version 16.

RESULTS

Of the 480 female students, 460 (96%) returned the questionnaires. Out of the returned forms, 286 (62%) were from medical, 96 (21%) from engineering, and 78 (17%) from the general university female students as shown in figure1. The respondents were of 18 to 25 years, from various socioeconomic strata, and 74 (16%) of them were married. Amongst them, 299 (65%) reported experiencing harassment in the form of sexual comments, jokes, gesture, looks and being touched, grabbed or pinched in a sexual way, invited for outing; and dire consequences for not indulging in 'friendly' relations (table No. 1) regardless of their appearance, attire and residential area. A majority (n=373, 81%) had to face this situation very frequently. The unmarried women more often experienced harassment than married women. None of them reported a serious sexual assault.

In a majority (64%), they were harassed by strangers, who included patients, attendants, visitors and passersby, followed by the fellow students (37%), faculty / teachers (32%) and the staff working there (2%) as shown in table # 2. The harassers' age varied from 18 to 60 years.

Many a times they had ignored mild forms of sexual harassment (e.g., jokes or teasing of a sexual nature). They (n=193, 42%) also were afraid of powerful position of the harassers.

Surprisingly 175 (38%) of the victims blamed themselves for what had happened, with a belief that they would not have experienced sexual harassment, if they had looked or dressed differently or even behaved differently.

Among these victims, 28 (6%) reported the incident to the family, 51 (11%) to the head of their institution, and 188 (41%) discussed with their friends/class fellows; while the rest 193 (42%) were afraid to discuss / disclose and felt small and depressed. These victims (48%) felt very uncomfortable, and frightened to move about in the college/university campus without a friend accompanying them. They were dependent on their family members, spouses, and friends.

The complaints were made against the fellow students, patients' attendants and the staff. The action was taken in the form of a verbal warning, and in case of attendants, their patients were discharged from the hospital. Although almost all of the participants (98%) wanted a punishment for the harassers, yet they (78%) were reluctant to disclose the name / identity of those perpetrators because of the fear of exploitation, social taboo, further embarrassment, adverse consequences, career obstacles, no action / response, and also because they (26%) considered it as a norm in the male dominated society. Among the victims, 166 (36%) reported feelings of powerlessness, humiliation, disbelief, shock, anger, fear, anxiety and depression, and the studies / academic activities of 105 (23%) were badly affected; and 51 (11%) had transient suicidal tendencies.

According to the 386 (84%) of the study participants, this issue should be taken seriously and awareness campaign must be carried out through various media.

Eighty nine percent of the respondents believed that almost all the females are harassed irrespective of their appearance and status. According to them, the reasons behind the female harassment included psychological problems, fun / joke, show power and authority, lack of respect for women, sexual perversion, inferiority complex of male counterpart, and dislike against working women.

Figure 1: **The Place of Study of the Research Participants**

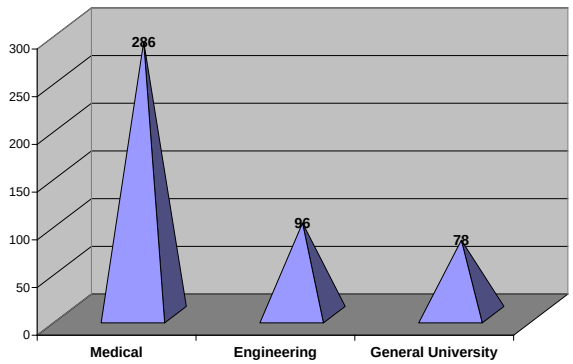

Table No. 1: Type of Sexual Harassment as reported by the Study Participants

Admired figure / dress in a sexual way	419 (91%)
Told a dirty joke	358 (78%)
Buzzed filthy songs	377 (82%)
Made abhorrent calls on telephone	202 (44%)
Sent muddy SMS	212 (46%)
Offered lift in his car	83 (18%)
Invited for outing or going to a restaurant	87 (19%)
Tried to show pornographic material	97 (21%)
Tried to talk about some vulgar movie or a TV programme	161 (35%)
Took interest in her personal life with the negative intention	313 (68%)
Tried to talk about her or his own sexual life	124 (27%)
Tried to have body touch while passing by / sitting / working / giving something / praising her work / teaching	414 (90%)
Tried to make her sit with him on some lame excuses	166 (36%)
Assured promotion / grades / other benefits for his bad intentions / demands	175 (38%)
Threatened for dire consequences if she did not make him 'friend'	51 (11%)
Tried to kiss	37 (08%)

Table No. 2: The Harassers as identified by the Study Subjects

Harassers	Frequency	
	Number	Percent
Strangers	294	64
Fellow Students	170	37
Faculty / Teachers	147	32
Staff	09	02

DISCUSSION

Sexual harassment in Pakistan frequently occurs in co-education institutions, public places (e.g., bus stops, markets, stadiums, cinema halls, parks, and females' college gates, etc.). The harassers include males of all ages belonging to different socioeconomic strata of the society.[9]

The study results showed that 65% female students were harassed on the basis of gender. This suggests that whether recognized or not, sexual harassment persists in the educational institutes and is a giant but silent problem of our society. Another study revealed that more than 50% medical students in Pakistan faced bullying or harassment.[10] Such a mess is also prevalent in other countries as females faced harassment at workplace or educational institutes. A study in the United Kingdom also reported that 1 in 3 female staff was harassed there.[11]

The harassers were strangers (patients, attendants, visitors and passersby), the fellow students, faculty / teachers and the staff. Because of routine practice of harassment, they could be unaware that their behavior was offensive or constitutes sexual harassment as was also found in other studies.[12]

It is a general concept that use of a particular clothing / dressing and outlook / appearance has an association with harassment issue.[13] This study denied any connection between harassment and attire and appearance of women. The problem of sexual harassment is not confined to any social strata. Although some women may be more vulnerable to sexual harassment than others, yet no woman seems to have immunity on the basis of her social status.

It has been found that marital status is related to the experiences of sexual harassment; with unmarried women more often experiencing harassment than married ones.[14,15,16] The same was reported in this study.

The facts that first or the first several harassing events are often ignored and the harassers are more powerful, physically and organizationally, than the victims, were also found in other studies.[17,18]

In many cases, the sexual harassment primarily is a manifestation of power, rather than sexual attraction. The females may be prone to harassment because of the male-dominated setup as is evident in our study. Such society structure usually has fewer women to demonstrate that they are equally proficient as males in all fields.[19]

As in our study the same was reported that the female students took somebody along with them if they had to see their supervisors who harassed them. This strategy is quite common among female students as well as working women.[20]

Generally the harassed women become mistrustful of men and thus become excessively dependent on their family members, spouses, and friends.[21]

Self-blame by the victims as reported in this study was found by others also. In Pakistani culture, the women are made to feel responsible for their own victimization by being told that if a man harasses them, it is because they have been doing something to provoke him.[8,22]

Reluctance shown by the victims to report harassment as found in this study, because they were ashamed, blamed themselves, frightened of further humiliation and they believed that they would not be taken seriously, is also evident from other studies.[25]

In general, harassment victims do not make complaints, as they feel that making a complaint will not accomplish anything, they are concerned about retaliation for complaining, and they fear that complaining might negatively affect them / family.[26]

According to many researches, victims were more willing to report harassment to their friends than to any other group; fewer victims would report to their department head or administrators.[27,28] The victims

recommended more assertive strategies to others than they would employ themselves.

In order to cope with the sexually harassing situations the harassed women respond in two ways i.e. "internal" or "external" in nature. The internal strategies are the attempts to manage the cognitions and emotions associated with the event (e.g., detachment, denial, relabelling, illusory control, and endurance); and the external strategies focused on the harassing situation itself (e.g., avoidance, assertion/confrontation, seeking institutional/organizational relief, social support, and appeasement.[23,24]

The results are same as found in other research. The victims vary in their emotional and behavioral responses to sexual harassment. Some deny its existence or importance. Others react with disbelief, shock, and/or doubt to even the most blatant acts; some feel sympathy toward their harassers. Many blame themselves and feel responsible to prevent the incident. Fear of resisting or reporting is a common response to sexual harassment; feelings of powerlessness are related to this fear. Self-esteem and confidence in both academic work and personal relationships are likely to plummet. Victims find themselves mistrustful of men in general. Additional emotional responses include anger, fear, irritability, depression, and feeling of humiliation and alienation, and a sense of helplessness and vulnerability. Any or all of these emotions may result in decreased concentration and drive and general listlessness, and also substance abuse and may result in serious mental health disorders.[29,30] The study participants also reported same feelings and suffered from mental agony and their performance was adversely affected. Those who reported suicidal tendencies could have experienced serious form of sexual harassment.

CONCLUSION

Sexual harassment seems prevalent at varying degree and in various forms in higher level educational institutes. This often occurs in unequal power relationship like workplaces or educational institutions. Many cases go unreported. The victims are reluctant to talk against their agony because of the fear of humiliation for themselves and their families. There is a need to sensitize the society to tackle this issue seriously, and mass awareness programs should be carried out through variety of media.

In Pakistan, this issue is yet to be acknowledged and investigated.

Limitation of the study: The findings can not be generalizable because of non-representative sample, as only those female students were included who volunteered to participate. Those who refused to respond could have suffered more severely but did not want to disclose because of further embarrassment.

Acknowledgments: The authors acknowledge the assistance of Fahmida Khatoon, Lecturer and Bismah Siddiqui, Nida Usmani, Arham Abbas, Anam Javed, Fatima Jaffrei, Nimra Iftikhar and Syeda Uroj, students of Dow International Medical College / Dow University of Health Sciences; whose tireless efforts made the data collection process possible.

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Original Article

Surveillance of antibiotic susceptibility patterns among Shigella species in stools of diarrheal children

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ABSTRACT

Objective: The objective of the present study was to findout the frequency of Shigella spp. in diarrheal patients in Pakistan and the susceptibility of isolated Shigella to different antibiotics: ampicillin, nalidixic acid, meropenem, tetracycline, amikacin, azactam, ciprofloxacin and chloremphenicol.
Design of Study: Experimental Study.
Place and Duration of Study: This Study was conducted at Pediatric Department, Mayo Hospital, Lahore and study was approved by Pakistan Pediatric Association.
Materials and Methods: Stool samples were collected from 50 diarrheal children less than five years of age who were admitted in the Paediatric Department Mayo Hospital Lahore, Pakistan. The samples were cultivated on standard media for Shigella, and Enterobacteriaceae. Susceptibility of Shigella isolates was tested by disk method.
Results: The frequency of isolation was 80% for Shigella species and 20% in others. Shigella. dysenteriae (65%) was the most frequently isolated species, followed by S. flexneri (23%), S. boydii, (10%) and S. sonnei (5%). All Shigella isolates were 100% sensitive to amikacin, azactam and ciprofloxacin, while multiple drug resistance patterns were observed by all four isolates to other antibiotics.
Conclusions: Shigella resistance is increasing against most commonly used antibiotics. Now it is the time not only to explore new drugs but also to invoke awareness about the hazards of unhygienic conditions and self medication.
Key words; Antibiotics, susceptibility, Shigella species, Diarrhea Children, Serotyping

INTRODUCTION

In developing countries, diarrhea is considered to be the major causes of childhood morbidity and mortality. About one billion episodes and 3.3 million deaths occur each year among children under five years of age. This ratio is highest in summer[1]. Overall, these children experienced on an average 2.6 episode of diarrhea per child per year. About 80% of children died of diarrhea in the first two years of their life. Epidemics are usually transmitted occur due to contaminated food and water in crowding area with poor sanitary conditions[2]. Flies are considered to play a major role in the spread of Shigella because of the low infective dose needed to cause diarrhea[3].

Almost all over the world 5 to 10% of dysentery and diarrheal diseases are caused by Shigella pathogens[4]. Diarrhea caused by bacteria Shigella is called Shigellosis and it is the causative factor of diarrhea among young children in developing nations[5]. Shigellosis is an acute gastroenteritis caused by Shigella dysenteriae, Shigella flexneri, Shigella boydii and Shigella soneii [2].

Shigellosis symptoms ranges from abdominal pain, cramps, fever, vomiting to bloody diarrhea and mucus contaminated stool. Some strains produce enterotoxin and shiga toxin. Infections are associated with mucosal ulceration, rectal bleeding and drastic dehydration. Fatality may be as high as 10 to 15 % with some strains[6]. The epidemiology and antibiotic susceptibility of Shigella species changes with the passage of time.

Despite the disease being self-limiting, antibiotic treatment is recommended because it reduces the duration of illness and the transmission rate of the disease by shortening the period of excretion of the pathogen[7]. Appropriate antimicrobial therapy of Shigellosis shorten the duration of fever and it apparently also reduces the risk of developing complications. Significantly reducing the spread of infections but constant use of antibiotics can increase the antibiotic resistance of Shigella sp which can cause major problem. Emergence of multiple drug resistance to cost effective antibiotics against Shigella is a matter of concern for the health authorities in developing countries[8].

The rapid emergence of multidrug-resistant (MDR) strains is largely due to their ability to acquire and disseminate exogenous genes associated with mobile genetic elements such as plasmids, transposons, integrons, and genomic islands[9]. Antibiotic resistance in enteric pathogens is of great concern in developing countries due to indiscriminate use of antibiotics. As Shigella are predominate isolates and show resistance to ampicllin but susceptibility to chloramphenicol with the exception of S. flexneri (susceptible to gentamicin)[10]. Some Shigella strains show resistance to

vibramycin, tetracycline and sensitivity against nalidixic acid, norfloxacin, chloramphenicol, amikacin and aztreonam[11]. Some of the Shigella strains are susceptible to ciprofloxacin and ceftrixone[12].

In Pakistan, self medication and purchase of drugs without prescription is common practice. Thus there is a greater possibility of development of resistant strains due to overuse of antibiotics[13]. The main objectives of this study were to isolate Shigella species from stool samples of diarrheal children of under five year of age and to find out the resistance and susceptibility of Shigell species against different antibiotics.

MATERIALS AND METHODS

Total fifty stool samples were collected in sterile wide mouth containers and rectal swabs from less than five year age group diarrheal children from Pediatrics Department of Mayo Hospital, Lahore, Pakistan. Selenite F broth and specific O (somatic) antigen were used for growth and cauterization of bacterial strains. Stool samples were streaked on SS agar (Salmonella-Shigella) and inoculated in Selenite F broth for sub-culturing and incubated for 24 to 72 hours respectively. Pathogens were identified as they formed colorless colonies on SS agar [14](Ellen et al.).

Characterization of strains

The isolates were characterized by performing conventional bacteriological and biochemical methods[15].

1. Gram's staining
2. Triple sugar iron agar test
3. Citrate utilization test
4. Indole production test
5. Manitol test
6. Urease test

Serotyping

Shigella are composed of four species or serogroup that are referred by A, B, C and D. Serogroup A refers to S. dysenteriae, B refers to S. flexneri, C corresponds to S. boydii and D to S. soneii. Shigelal species were confirmed with polyvalen (serogroup A-D) antisera. Shigella isolates tested by slide agglutination with polyvalent A-D Shigella antisera. Isolates that agglutinate with antisera were reported as presumptive Shigella species[16].

Antibiogram pattern

Antibiogram pattern of isolated strains were determined on Mueller- Hinton agar. Each culture to be tested for antibiotic susceptibility was streaked onto non inhibitory agar medium. For comparison, the anti microbial susceptibilities of isolates from the standard culture were determined by standard disk method. E. coli American Type culture collection (ATCC). Zones of inhibition were determined with the help of list break points of antibiotics[17].

RESULTS

In present study, total fifty stool samples were collected from diarrheal children of less than five year age. Out of 50, 32 were boys (64%) and 18 were girls (36%). Stool samples were collected as *Shigella* is largely excreted through stool. *Shigella* was isolated from a number of commercially prepared plating media used with members of Enterobacteriaceae. *Shigella* species were isolated in 40 samples (80%) and 10 samples contained other members of Enterobacteriaceae (20%) such as *Salmonella* and *E.coli.* All pathogenic forms of *Shigella* were confirmed upto species level by serotyping. All *Shigella* isolates were tested by slide agglutination with polyvalent A-D *Shigella* antisera. Out of forty, 26 (65%) were *S. dysenteriae*, 8 (23%) were *S. flexneri*, 4 (10%) were *S. boydii* and 2(5%) were *S. soneii*. Boys and girls have different rate as presented in Table No.1.

Table No.1: Prevalence and frequency of different bacteria isolated from diarrheal patients

Bacterial species	Number	Boys	Girls
S. dysenteriae	26	17	9
S. flexneri	8	6	2
S. boydii	4	1	3
S. soneii	2	2	0
Others	10	6	4
Total	50	32	18

Identification of selected bacterium

The isolated bacterium was subjected to Gram's staining to screen Gram negative, non capsulated shape and colorless growth. Biochemical tests for identification of selected strain were performed. Results obtained from these tests are given in table No. 2.

Antibiogram pattern

Antibiogram pattern of isolated strains were determined on Mueller- Hinton agar. Commercially available anti-microbial disks were used and incubated at 37 ºC for 24 hours on agar. Zones of inhibition were measured in each case. Most of *Shigella* isolates in the study were found resistant to meropenem and tetracycline and sensitive to amikacin, azactam and ciprofloxacin. Two antibiotics (Chlorempheniсol and Nalidixic acid) showed resistance to *S. dysenteriae* and sensitivity to others strains (Table No.3)

Table No. 2: Biochemical characterization of bacterial strains isolated from diarrheal patients of less than five year of age

Bacteria	Shape	Gram's staining	Manitol	TSI	Citrate test	Ind Test	Urease test
Shigella	Rod	-ve	-	Slant Alkaline Butt Acidic	-ve	-ve	-ve
S. dysenteriae	Rod	-ve	No change	Slant Alkaline Butt Acidic	-ve	-ve	-ve
S. flexneri	Rod	-ve	Acid production	Slant Alkaline Butt Acidic	-ve	-ve	-ve
S. boydii	Rod	-ve	Acid production	Slant Alkaline Butt Acidic	-ve	-ve	-ve
S. sonnei	Rod	-ve	Acid production	Slant Alkaline Butt Acidic	-ve	-ve	-ve

Table NO.3: Susceptibility of antibiotics against different *Shigella* species

Antibiotic used	*S. dysenteriae*	*S. flexneri*	*S. boydii*	*S. sonnei*
Amikacin	S (8%)	S (2%)	S (1%)	S (0.5%)
Azactam	S (10%)	S (3%)	S (2%)	S (0.5%)
Ampicillin	S (5%)	S (1%)	R (0.5%)	R (0.5%)
Chloramphenicol	R (5%)	S (2%)	S (2%)	S (1%)
Ciprofloxacin	S (17%)	S (6%)	S (2%)	S (0.5%)
Meropenem	R (3%)	R (2%)	R (0.5%)	R (0.5%)
Nalidixic acid	R (15%)	S (5%)	S (1%)	S (1%)
Tetracycline	R (2%)	R (2%)	R (1%)	R (0.5%)

DISCUSSIONS

The aim of the present study was to isolate Shigella sp. from fecal samples of diarrhea children less than five years of age. It has been reported that worldwide acute diarrhea disease is the second cause of death among all infectious diseases in children younger than 5 years of age [18]. Total 50 stool samples were collected and subjected to medias for bacterial growth. All isolated species were subjected to Gram's staining and biochemical tests for identification of species. Out of 50 samples 40 contained Shigella sp. and were Gram's negative, rod shaped, with colorless growth and non capsulated. Remaining 10 were belonging to Enterobacteriaceae such as Salmonella and E.coli. It was found that S. dysenteriae was more frequently prevailing strain (65%) than other three after serotyping and boys were more victims of Shigella as compare to girls as given in Table 1. Our findings are combatable with previous studies by Kausar et al.[13] who studied frequency of Shigella species and found to be more frequent (19.1%) and S. dysenteriae was more common than other three strains. Biochemical tests showed different results presented in Table 2. These results are in accordance with findings of Uzma et al.[11] they observed Shigella isolates and found indole test to be negative, oxidase negative, citrate negative, urease negative while TSI as positive.

Antimicrobial therapy is recommended for shigellosis as it can shorten the severity and duration of illness, reduce shedding of the organism, and prevent secondary complication and death. However antimicrobial resistance occurred among Shigella species, since1940s, when sulfonamide resistance among Shigella organism was first detected in Japan 19. In our study, all four isolates showed multiple drug resistance patterns (Table 3). Drug susceptibility of S. dysenteriae showed that their resistance to nalidixic acid, cholramphenicol, tetracycline and meropenem but showed their sensitivity against amikacin, azactam, ciprofloxacin and ampicillin. These results are in conformity with findings of Atif et al.[20] they studied S. dysenteriae S and E. coli resistance against commonly used antimicrobial agents i.e. amoxicillin, chloamphenicol, tetracycline, cotrimoxazole, nalidixic acid, sulfonamide and neomycin and sensitive to amikacin, azactam and ciprofloxacin. S. flexneri isolates were resistant to meropenem and tetracycline while these were found sensitive to nalidixic acid, cholramphenicol, amikacin, azactam, ciprofloxacin and ampicillin. The previous findings quoted by Uzma et al.[11] also showed the same trend, hence substantiates our results.

Antibiotics susceptibility of S. boydii showed resistance to ampicillin, tetracycline and meropenem but give susceptibility towards nalidixic acid, cholramphenicol, amikacin, azactam and ciprofloxacin. These are in conformity with the findings of Urio et al.[10] they also found S. boydii resistant to ampicillin, sulphtriad and cepalothin. Ciprofloxacin and chlorempheniol were the most effective antimicrobial agents against S. boydii.

In our study it was also seen that S. sonii were resistant to ampicillin, tetracycline and meropenm while

susceptible to amikacin, azactam, nalidixic acid, ciprofloxacin and chloremphenicol. These results are in line with Isenbarger et al.[21]studies as they also found S. sonii strains resistant to ampicillin and meropenem and susceptible to nalidixic acid, ciprofloxacin and chloremphenicol.

CONCLUSIONS

It can be concluded from the present study, in heavily populated areas of Pakistan, ecosystem contains high background level of faecal population associated with the transmission of enteric pathogens through water, food, human and animals. In presence of these factors gastroenteritis remains one of the major health problems. *Shigella* resistance is increasing against most commonly using antibiotics. Exploring of new drugs and to inculcate hygienic awareness among the mass is need of the day. Self medication and purchases of drugs needs to be under legal cover.

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Original Article

A Comparative Study On Liver Toxicity Profile Of Diclofenac Sodium and Piroxicam on Rabbits

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ABSTRACT

Objective: Aim of this study was to determine the clinical hepatotoxicity of diclofenac sodium and of piroxicam, and to evaluate whether these drugs could elicit liver cell destruction and anemia, and which drug is comparatively safer for prolong use.

Place and Duration of Study: This study was conducted in the department of Pharmacology, Faculty of pharmacy, University of Karachi, Karachi. Duration of study was 30 days.

Materials and Methods: Male 40 rabbits were equally divided into 4 groups, group A was served as control and the group B & C was diclofenac sodium (0.8mg/kg/day and 1.5mg/kg/day), and group D was of piroxicam (0.31 mg/kg/day) treated. All the animals were caged in pair in an iron caged with free access to grass and hay of standard diet and tap water for a period of 30 days. Diclofenac sodium in 2 different doses 0.8mg/kg/day, 1.5mg/kg/day and similarly Piroxicam (0.31mg/kg/day) dissolved in drinking water and was given orally for a period of 30 days. Control rabbits were given tap water. At the end of 30 days blood was collected through cardiac puncture from each rabbit and was analyzed to determine the levels of SGOT, SGPT, Bilirubin, ESR and Erythrocyte count.

Result: It was found that these drugs can induce severe hepatic damage but the ratio of liver toxicity is different, as evident by the elevation of serum aminotransferases, bilirubin and changes in hematological profile. The experimental results suggest that SGOT and SGPT levels were significantly increased in diclofenac sodium treated rabbits after 10 and 30 days ($P < 0.01$), while piroxicam treated rabbits showed significant result, ($P < 0.05$) only after 30 days of treatment.

The level of bilirubin was significantly increased in diclofenac sodium treated rabbits after 10 days and 30 days ($P < 0.01$) and piroxicam also showed significant result ($P < 0.05$) after 30 days treatment. Erythrocyte count decreased in both control and treated rabbits after 10 days but control results are not significant. After 30 days diclofenac sodium showed highly significant decrease in count of erythrocytes ($P < 0.01$), but piroxicam showed less significant results ($P < 0.05$). E.S.R values significantly increased in diclofenac sodium and piroxicam treated rabbits after 10 days and 30 days.

Conclusion: It can be concluded that diclofenac sodium and piroxicam both can play a role in inducing hepatocelllualr damage, but a greater increase in liver toxicity was seen in diclofenac sodium treated rabbits rather than piroxicam treated rabbits.

Key words: Diclofenac Sodium, Piroxicam, Hepatotoxicity, serum aminotransferases, Bilirubin.

INTRODUCTION

Pain is an unpleasant sensory and emotional experience, and one of the greatest services is to acquire skill in the management of pain. Analgesics are drugs that relieve pain and among them non-narcotic analgesics are those which act peripherally to achieve this effect[1]. When a tissue is injured or stimulated, there is increased synthesis of prostaglandins which act as mediators of inflammation, and a drug that prevents the synthesis of these is likely to be affective in relieving pain[2]. Non-steroidal anti-inflammatory drugs (NSAID's) are among the most widely used medications in the world because of their demonstrated efficacy in reducing pain and inflammation[3]. Their efficacy has been documented in a number of clinical disorders, including osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, gout, dysmenorrhea, dental pain and headache[4,5]. The basic mode of action is inhibition of the pro-inflammatory enzyme cyclooxygenase (COX). NSAID's as a class comprise both traditional nonselective NSAIDs, which nonspecifically inhibit both COX-1 and COX-2, and selective COX-2 inhibitors. Although effective for relieving pain and inflammation, NSAID's are associated with a significant risk of serious gastrointestinal adverse events with chronic use[6]. The use of analgesics has increased considerably and had led to the knowledge of some serious unwanted hepatotoxic effects of some commonly used NSAID's. Present study is designed to investigate the effects of Diclofenac sodium and piroxicam when administered for different duration and with different dosages[7].

Diclofenac and piroxicam are relatively nonselective cyclooxygenase inhibitors, have been widely used to treat inflammatory or nociceptive disorders such as rheumatoid arthritis, osteoarthritis, cervicobrachial syndrome, frozen shoulder and post operative pains[8] . Whereas these NSAID's when used in long term chronic diseases can cause liver damage with elevation of liver enzymes[9].

An elevation of ALT or AST was observed in patients receiving diclofenac when compared to other NSAIDs. Transaminase elevations were seen more frequently in patients with osteoarthritis than in those with rheumatoid arthritis. In addition to enzyme elevations seen in clinical trials, post marketing surveillance has found rare cases of severe hepatic reactions, including liver necrosis, jaundice, and fulminant fatal hepatitis with or without jaundice. Some of these rare reported cases underwent liver transplantation[10]. Diclofenac was found to generate protein adducts in the livers of treated mice as well as in rat hepatocytes via protein acylation by the drug glucuronide**.** In vitro experiments with cultured rat hepatocytes have shown, however, that the covalent binding of diclofenac is neither the only nor the major cause of acute cytotoxicity**.** Moreover, it is also suggested that diclofenac is more cytotoxic to rat hepatocytes than piroxicam due to cytochrome P-450 (CYP)-mediated metabolism**,** by the formation of reactive metabolite(s) by drug oxidation, which could be related to drug toxicity, has been reported. While piroxicam can cause liver damage in high doses by an immunoallergic mechanism & formation of ductopenia, but factors responsible for this chronic evolution are still unknown[11,12].

The objective of the present study is to determine the role of diclofenac sodium & piroxicam in inducing hepatocellulr damage, further to evaluate whether these drugs could elicit liver cell destruction and anemia, and which drug is comparatively safer for prolong use.

MATERIALS AND METHODS

- Locally bred 40 male rabbits weighing range 1.03 to 1.7kg were used for the experiment. They were caged in pair in an iron caged with free access to grass and hay of standard diet and tap water. Food intake was monitored weekly by giving rabbit's weighed amount of food and weighing the remaining food in the iron cage. Body weight, food intake, water intake, skin color and posture of all rabbits were monitored in pre-experimental period.

Drug Administration

Diclofenac sodium in 2 different doses 0.8mg/kg/day, 1.5mg/kg/day and similarly Piroxicam 0.31mg/kg/day dissolved in drinking water and was given orally. Control rabbits were given tap water. In the beginning of the experiment 40 rabbits were divided in to 4 groups, and labeled as:

1. Water treated (control).
2. Diclofenac sodium 0.8mg/kg/day treated.
3. Diclofenac sodium 1.5mg/kg/day treated.
4. Piroxicam 0.31mg/kg/day treated.

Blood was collected through cardiac puncture from each control rabbit in sodium citrate containing test tubes. Centrifugation method was used to obtain plasma. Plasma, samples were stored at 2-8^{o}C for the estimation of SGOT, SGPT, Bilirubin, ESR and Erythrocyte count.

The dosing was started from day 1 till day 30th. At 10th day after the dosing, body weight, food intake, water intake, behavioral monitoring and blood samples were collected in 3.8% sodium citrate containing test tubes by cardiac puncture. Centrifugation gave plasma, which was used for the different tests.

On 30th day of the dosing, body weight, food intake, water intake and behavioral monitoring, rabbits were sacrificed and blood was collected in 30 different 3.8% sodium citrate (anti-coagulant) containing test tubes. Blood was centrifuged and plasma was collected to perform the tests.

After separation of serum, liver enzymes SGOT, SGPT & Bilirubin were estimated by Spectrophotometer by using standard kit method. E.S.R is estimated by Westergen's tube method & RBC's count by Haug method.

Statistical analysis

Comparison of difference of mean between diclofenac sodium in two different doses, control group & piroxicam was made by using student's t-test. Rabbits liver enzymes like SGPT, SGOT and Bilirubin and blood parameters like E.S.R and Erythrocyte count, after 10day and 30day were statistically analyzed by two way ANOVA using a software "Minitab-15". A p value less than 0.05 were considered statistically significant and p value less than 0.005 were considered highly significant.

RESULTS

Figure No. 1: Shows the effect of diclofenac sodium at the dose of 0.8 and 1.5 mg/Kg/day and 0.31mg/kg/day piroxicam on rabbit liver enzyme SGOT and SGPT (U/I). Data analyzed by two-way ANOVA (df = 1, 36), shows that SGOT and SGPT were significantly increased ($P<0.05$) in diclofenac sodium 0.8 and 1.5mg/Kg/day treated rabbits after 10 days and highly significant ($P<0.01$) results obtained in rabbits after 30 days. But piroxicam 0.31mg/Kg/day treated rabbits show ($P<0.01$) significant effects only after 30 days of treatment.

Figure No.2: Show the effect of diclofenac sodium and piroxicam on rabbit Erythrocyte count & ESR. Fig 2a

Shows effect of o.8mg/Kg/day, 1.5mg/kg diclofenac Na & 0.31mg/kg piroxicamon rabbit Erythrocyte count after10 and 30 days. Data analyzed by two - way ANOVA (df = 1, 36), shows that erythrocyte count significantly increases (P<0.05) in diclofenac sodium 0.8 mg/Kg/day treated rabbits after 10 days and highly significant (P<0.01) results obtained in rabbits after 30 days, while piroxicam show less significant results after 10 days but significant results (P<0.05) after 30 days treatment.

And fig 2b shows effect of o.8mg/Kg/day, 1.5mg/kg diclofenac Na & 0.31mg/kg piroxicam on rabbit ESR after10 and 30 days. That also show highly significant results (P<0.05) after taking both diclofenac sodium and piroxicam for10 days, and highly significant results (P<0.01) obtained after 30 days.

Figure No. 1: Effect of Diclofenac Sodium 0.8mg/Kg 1.5mg/Kg & Piroxicam 0.31mg/Kg on Rabbit Liver Enzyme Sgot & Sgpt (U/I)

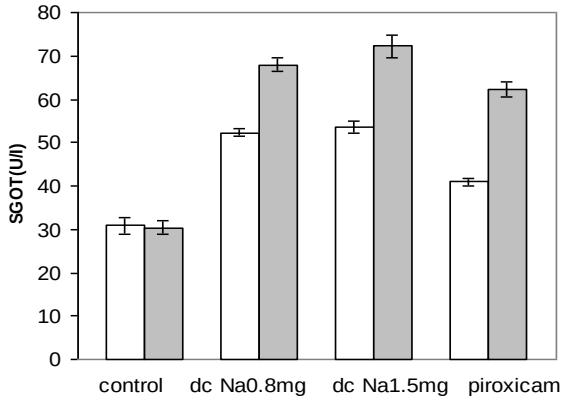

Figure No.1a

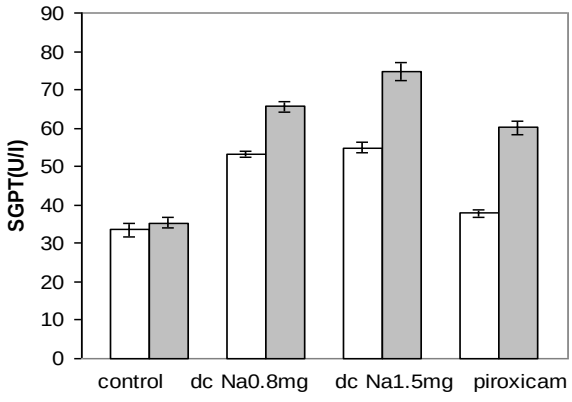

Figure No.1b

Figure 1: Effect of diclofenac sodium & piroxicam on rabbit liver enzymes SGOT & SGPT.

Figure 1a: Shows effect of o.8mg/Kg/day diclofenac Na, 1.5mg/Kg/day diclofenac Na & piroxicam on rabbit liver SGOT after10 and 30 days, while Figure 1b: Shows effect of diclofenac sodium 0.8mg and 1.5mg/kg/day and piroxicam 0.31mg/kg/day on rabbit liver SGPT after10 and 30 days,

Figure No.2: Effect of Diclofenac Sodium 0.8mg/Kg , 1.5mg/Kg & Piroxicam 0.31mg/Kg on Rabbit Erythrocyte Count /Mm^3& Esr(Mm)

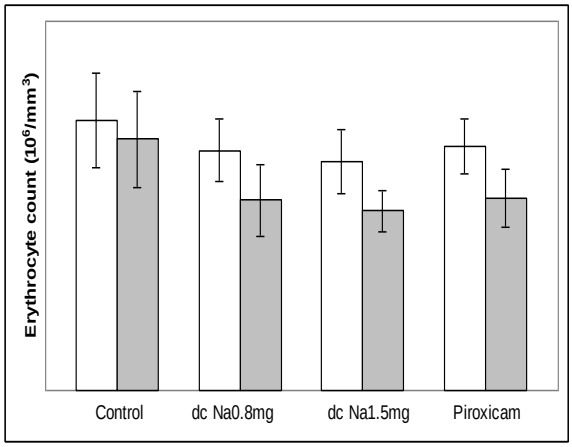

Figure No. 2a

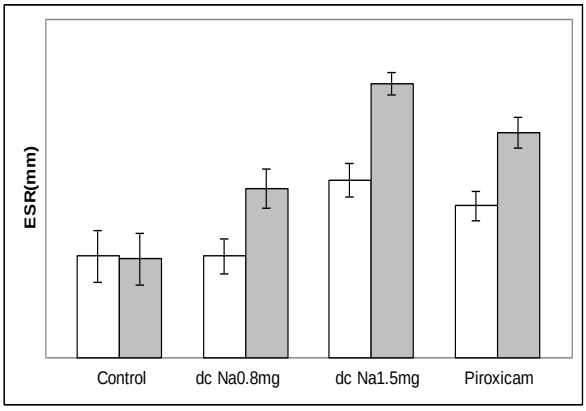

Figure No. 2b

Figure No. 2: Effect of diclofenac sodium and piroxicam on rabbit Erythrocyte count & ESR.

Figure No. 2a Shows effect of o.8mg & 1.5mg/kg/day diclofenac Na and 0.31mg/kg/day piroxicam on rabbit Erythrocyte count after10 and 30 days.

Figure No. shows effect of 0.8mg & 1.5mg/Kg/day diclofenac Na and 0.3mg/kg/day piroxicam on rabbit ESR count after 10 and 30 days.

Table No.1: Show the effect of diclofenac sodium at the dose of 0.8 and 1.5 mg/Kg/day and 0.31mg/kg piroxicam on rabbit Bilirubin (mg/dl).). Data analyzed by two-way ANOVA (df = 1, 36), shows that Bilirubin significantly increases (P<0.05) in diclofenac sodium 0.8 and 1.5mg/Kg/day treated rabbits after 10 days and highly significant (P<0.01) results obtained in rabbits after 30 days. Piroxicam 0.31mg/kg/day treated rabbits show (P>0.05) insignificant effects after 10 days but highly significant effect (P<0.01) after 30 days treatment.

Table No.1: Effect of Diclofenac Sodium 0.8mg/Kg , 1.5mg/Kg and Piroxicam 0.3mg/Kg on Rabbit Bilirubin (Mg/Dl)

	on Day 10	on Day 30	two-way ANOVA (df = 1, 36)
Control	0.4059 ± 0.129	0.478 ± 0.111	F-Interaction= 4.15, P <0.05
Diclofenac Na 0.8mg/Kg/day	0.5496* ± 0.094	0.761**± 0.09	
Diclofenac Na1.5mg/Kg/day	0.913**± 0.16	1.147**± 0.162	
Piroxicam 0.31mg/Kg/day	0.5729*± 0.035	0.93**± 0.061	

Values are mean ± S.D. (n=10). Significant differences by Newman-Keuls test *p<0.05 is significant & **p<0.01 is highly significant, as compared to control rabbits, following data analyzed by Two Way ANOVA df (1,36).

DISCUSSION

The drugs that are used as analgesic and anti-inflammatory agents are usually used as over the counter drugs. This implies to a fact that there is no check as to whether the patient is using rationally or irrationally these drugs in different inflammatory conditions.

Diclofenac sodium & piroxicam are n**on**-steroidal anti-inflammatory drugs (NSAIDs) used for most rheumatic disorders, and are used in large numbers as anti-inflammatory and analgesics, both as prescripti**on** drugs and over the counter purchases. The epidemiological risk of clinically apparent liver injury is greater (200 cases per 100 000 patient years) from diclofenac sodium than piroxicam (1–8 cases per 100 000 patient years), but when it occurs, it can be serious and can cause diagnostic c**on**fusi**on**. The adverse effect profile needs to be studied [13,14]

Diclofenac can impair ATP synthesis by mitochondrion which is in accordance to our result indicating that they can cause hepatotoxicity over long period of administration of these drugs. When we administered diclofenac in the dose of o.8mg/kg and 1.5mg/kg both profile show that the level of SGOT and SGPT were significantly elevated. The toxicity may be related to the impairment of ATP synthesis and also by impairing NADPH which are required to reduce the toxicity of hepatocytes.

This toxicity is also related to a fact that diclofenac sodium can form a toxic metabolite, and can also cause binding of drug to hepatic proteins[15].

The toxic metabolite formed is 4'hydroxy diclofenac by the action of CYP2CP[16].The results also showed that the toxicity profile of diclofenac sodium and potassium changed when the duration of therapy was increased. So the levels of SGOT and SGPT were further increased significantly after the period of 30 days dosing, thus indicating that the hepatotoxicity is not only dose dependent but is also duration dependent.

The changes in the liver enzymes i.e. transaminases were not only significant but also the level of bilirubin was found to be elevated after the administration of these drugs. This is also in accordance with results reported earlier[17] where jaundice was presented in a patient treated with diclofenac. The level of bilirubin increased indicates that the hepatotoxicity may be progressed towards liver necrosis. The toxic effects of diclofenac and its metabolites, along with hypersensitivity reactions may be the suggested molecular mechanism of liver injury.

The reason of marked elevated transaminases in the rabbits liver may be attributed to the fact that the metabolic pathways of diclofenac results in the formation of a metabolite that leads to acute lethal cell injury.

The increased level of bilirubin may also leads to certain renal dysfunctions as increased clearance and precipitation of bilirubin could lead to the renal nephritic syndromes. This finding may also be related previous study[18], who has reported that there may be renal complications due to the use of NSAID's particularly diclofenac partially due to the development of secondary membranous nephropathy. This was also supported by the study that the renal complications were reversed after the withdrawal of diclofenac and showed response if treatment with prednisolone was initiated.

The significant rise in the level of bilirubin could also be attributed to the findings that the total erythrocyte count and Hb was significantly reduced after the administration of diclofenac. The increased hemolysis of the R.B.C's can also lead to the increased level of bilirubin which could further be exaggerated by the liver toxicity, as liver could not decrease the concentration of bilirubin of serum through the clearance mechanism. As reported[19] that there may be revised forms of hepatic injury induced by diclofenac. In this type of injury there is a combined failure of canalicular pumps and other intracellular processes also that allow toxic bile acids to accumulate, causing secondary injury to hepatocytes. There may be also the likelihood to develop the injuries to the cells of the bile duct. The injury to the hepatocyte may occur due to the disruption of the intra-cellular calcium homeostasis that leads to the disassembly of acute fibrils at the surface of hepatocyte. This may result in blabbing of the cell membrane rupture, and cell lysis.

The other possible mechanism may involve the combination of the drug with enzyme that leads to the formation of adduct. These adduct then serve as immune targets which may migrate towards the surface of the hepatocyte where they can induce the formation of antibodies, leading to inflammation and neutrophil-

mediated hepatotoxicity. This further could lead to programmed cell death (apoptosis) with immune mediated injury destroying hepatocytes by way of tumor necrosis factor (TNF) and FAS pathways[19].

The reason of decreased count of erythrocytes with the elevation in the levels of serum tranaminases and bilirubin could also be due to the development of acute immune hemolytic anemia as reported by[20]. The drug development antibody can react with the R.B.C'$_s$ leading to hemolysis. Another finding by[21], shows that there may be the development of IgM antibody that react strongly with the R.B.C'$_s$. This antibody was developed by the metabolite of diclofenac metabolism i.e. 4-hydroxy diclofenac. This could also support our finding that possibly the formation of hydroxyl diclofenac has lead to the agglutination of R.B.C'$_s$ in the blood of the rabbit, that has elevated further the level of bilirubin and was the major cause of decline in R.B.C'$_s$ count due to mediated hemolysis.

The hepatotoxic drug reactions involve moderate to severe injury to hepatocyte and is indicated by a clinical picture that resembles viral hepatitis[19]. This is characterized by a rapid onset of malaise and jaundice in association with elevated aminotranferase level which may be at least 5 times as high as normal. This is consistent with our findings indicating the rise in the level of tranaminases was very significant and was indicative of liver toxicity. The rise in liver transaminases is so high that probably if the drug was not stopped that death could have been reported. This is also true because in the previous reports and investigations on diclofenac clearly indicate that the drug should be discontinued if the symptoms are to be reversed otherwise the toxicity may be further enhanced, and become fatal.

The finding also show that diclofenac sodium is more toxic as compared to piroxicam, since the level of transaminases were increased by diclofenac sodium even often 10 days of treatment, whereas piroxicam produces significant toxicity after 30 days of treatment. Piroxicam study indicates that there may be transient elevation of SGOT and SGPT in clinical trials of patients. The study also showed elevated levels of bilirubin, jaundice, hepatitis and liver necrosis. These studies are also in accordance to our results, but are also suggestive that the Oxicams may also be hepatotoxic but only if given for long duration and in high doses. This is also confirmed by the literature which indicates that Piroxicam should be used in the lowest effective dose for the shortest possible duration.

The NSAID'$_s$ diclofenac sodium was used in both therapeutic and high doses where as Piroxicam was only used in therapeutic doses, but since it was given over 21 days, that has lead to the appearance of toxic adverse effects.

The effect of Piroxicam on hemolysis and decline in Hb and Erythrocyte counts are also in relation to our findings since Piroxicam can produce anemia and it is required that Hb and hematocrit should be routinely checked[13].

Piroxicam can elevate the bleeding time and should be given with caution if patient is maintained on warfarin. This is also related to our finding since hepatotoxicity could lead to less formation of procoagulants. This effect could also elevate bleeding time and the combination of Piroxicam with aspirin and other platelet aggregators should be avoided or used with caution[22].. Piroxicam could lead to hepatitis with cholestasis and jaundice. The liver function and jaundice was resolved after discontinuation of Piroxicam, hence Piroxicam use also leads to hemolysis leading to jaundice and abnormal liver function indicated by elevated SGOT, and SGPT. The incidence of liver toxicity by Piroxicam is also affected by the dose, which is supported by the literature indicating that in patients with hepatic insufficiency the dose needs to be adjusted.

Recent in vitro animal studies have gone some way towards demonstrating the mechanisms of NSAID induced hepatotoxicity but further work is required to fully understand the pathogenesis. Currently there are no markers and tests neither to identify those at risk of NSAID-induced hepatotoxicity, nor to identify those likely to develop hepatic failure as opposed to deranged liver function tests. While hepatotoxicity related to NSAIDS is an uncommon adverse effect, it is important to be vigilant to the hepatotoxic potential of any NSAID, as increased awareness, surveillance and reporting of these events will lead to a better understanding of the risk factors and the pathophysiology of NSAID-related hepatotoxicity. This work further can be expanded to check the effect of diclofenac & piroxicam on cardiac enzymes and kidney associated enzymes to evaluate the different toxicity profile on vital organs, and we can also see the other hematological parameters and metabolic pathways like Carbohydrate and lipid metabolism for further investigations.

CONCLUSION

In summary diclofenac sodium and piroxicam both were found to have strong anti-inflammatory agents but piroxicam has lower hepatotoxic effect after prolong use rather diclofenac sodium.the lesser toxicity profile due to its long half life, The prolonged half-life (50 hours) results in the maintenance of relatively stable plasma concentrations throughout the day on once daily doses and to significant accumulation upon multiple dosing. Also the biotransformation products of Piroxicam metabolism are reported to not have any

anti-inflammatory activity. These finding suggest that piroxicam could be a clinically useful NSAID in chronic inflammatory diseases when taken in long term use.

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Original Article

Antimicrobial Susceptibility Testing and Esbl Detection from the Bacteria in Haemodialysis Patients

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ABSTRACT

Objective of Study: To find out the antimicrobial sensitivity and extended spectrum β-lactamase producing organisms among clinical isolates recovered from patients on haemodialysis. Extended spectrum β-lactamase are enzymes produced from some strains of gram negative bacilli that mediate resistance to extended spectrum cephalosporin and aztreonam. They are most common in E.coli and Klebsiella species but are present in variety of enterobacteriacea.

Design of Study: Experimental and observational study.

Place and duration of Study: This study was carried out in Microbiology Department of BMSI, JPMC, Karachi. This study was carried out from June 2005 to June 2006.

Materials and Methods: A total of 250 cases irrespective of age and gender were included in this study. A total of 15 gram positive cocci (7.5%) and 175 (87.5%) gram negative organisms were recovered. In this study 66.66% E.coli and 33.33% Klebsiella species were ESBL producing. Antimicrobial sensitivity pattern in this study show that most of the organisms were sensitive to 2nd and 3rd generation cephalosporins and fluroquinolones i.e. ciprofloxacin.

Results: Table 1 shows isolation of ESBL producing organisms from 200 positive cases. Out of these 175 cases were from Enterobacteriaceae, among these 06 (3.42%) cases have been found to be ESBL producing organisms.

Conclusion: The results of this study support the use of initial antimicrobial therapy to reduce the spread of infection and other complications. Currently ciprofloxacin is regarded as the drug of choice for the treatment of infection caused by both gram negative and gram positive bacteria in patients on hemodialysis

Key words: Extended spectrum β-lactamase (ESBL), antimicrobial sensitivity.

INTRODUCTION

Bacterial infections of all types seem to be increased in incidence, but there is a particular risk of infections related to vascular access sites or devices in patients on haemodialysis. Many of these infections are due to sepsis, primarily arising from the vascular access site. Septicemia alone accounts for almost 11% of mortality in hemodialysis patients. Hemodialysis patients are also a sentinel population for the emergence of antimicrobial resistance, especially with regards to gram positive cocci (vancomycin resistant enterococci (VRE), methicillin resistant Staphylococcus aureus (MRSA), Staphylococcus aureus with reduced susceptibility to vancomycin intermediate Staphylococcus aureus (VRSA), and methicillin resistant Staphylococcus aureus (MRSA)[1].

Antimicrobial use in concern with patient to patient transmission of resistant strain, has caused a rapid increase in prevalence of antimicrobial resistance in recent years. This particularly includes threat to dialysis patients who have often been at the fore front of epidemic of resistance[2].

Resistance to Beta lactam antimicrobial agents especially Extended spectrum cephalosporin and other agents among clinical isolates of gram negative bacteria is on the rise worldwide. The antimicrobial resistant pathogens include Extended spectrum cephalosporin resistant E.coli, Klebsiella pneumoniae, Enterobacter Coloacae, Serratia and Citrobacter friundii and Pseudononas aeruginosa and Acinitobacter banmnni[3].

The emergence of extended spectrum β-lactamase (ESBL) producing Enterobacteriaceae, particularly Escherichia coli and Klebsiella pneumoniae, presents significant diagnostic and therapeutic challenges to the management of infections due to these organisms[4].

MATERIALS AND METHODS

A total of 190 bacteria were recovered from intravenous catheter tips from patients admitted in different hospitals e.g. Nephrology unit of JPMC, Kidney centre and SIUT. The Samples received initially incubated on blood agar, MacConkey agar and Chocolate agar. The samples were incubated at 37ºC for 24 hours. The organisms were primarily identified by standard techniques. The antimicrobial sensitivity test done by standard National Clinical Committee Laboratory Standard (NCCLS) method **(**Linscott and Brown 2005**)[5].**

Extended spectrum beta-lactamase (ESBL) production was carried out by double disc diffusion method[6].

According to this method a susceptibility disc containing (Augmentin) Amoxicillin 10 µg+ Clavulanat acid 20 µg was placed in the center of plate containing Muller Hinton Agar. Amoxicillin 10 µg+ Clavulanat acid 20 µg (Augmentin) disc was placed as an inhibitor of beta-lactamase. Cefotaxime, Ceftazidim, Ceftriaxone and Azotreonam (30µg) each were placed at a distance of 30mm (center to center) from Amoxicillin 10 µg+ Clavulanat acid 20 µg (Augmentin).

Enhancement of inhibtion zone towards Amoxil + clavulanic acid disc indicating synergy of Clavulanic acid with anyone of the test antibiotics was taken as presumptive evidence of ESBL production. The quality control strains used for DDT or DDST testing were E-coli ATCC 25922 and Klebsiella pneumoniae ATCC 700603[7].

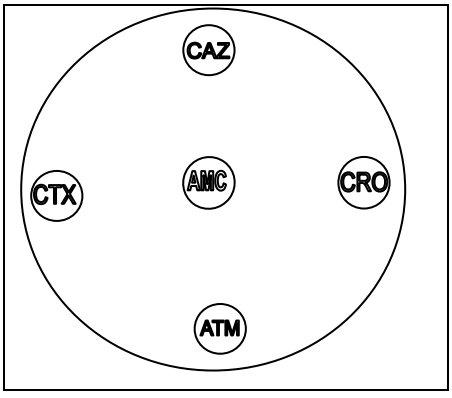
The following discs are applied on Muller Hinto Agar (MHA)

Disc	Concentra-tions	Oxoid disc code	Inhibition zone
Amoxil + clavulanic acid	20+10µg (C.A+Amp)		≥20
Ceftazidime	30µg	CAZ30	≤27
Cefotaxime	30µg	CTX30	≤27
Ceftriaxone	30µg	CRO30	≤25
Azactum	30µg	ATM30	≤27

Interpretation Results:

An organism was interpreted as containing an ESBL if there is an increase or extension of >5mm in the inhibition in the area between the Amoxicillin 10 µg+ Clavulanat acid 20 µg (Augmentin) disc and any one of the four cephalosporin discs in comparison with the zone of inhibition on the for side of that disc[6].

Muller Hinton Agar Plate With Antimicrobial Disc



- Diagram showing double disc diffusion (synergy) test used to detect the (ESBLs) Extended Spectrum Beta-Lactamase producing organisms (Jarliar et al., 1988) [4].

CAZ = Ceftazidime, CTX = Cefotaxime
AMC = Amoxicillin 10 µg+ Clavulanat acid 20 µg
CRO = Ceftriaxone, ATM = Aztreonum

RESULTS

Table 1 shows isolation of ESBL producing organisms from 200 positive cases. Out of these 175 cases were from Enterobacteriaceae, among these 06 (3.42%) cases have been found to be ESBL producing organisms.

DISCUSSION

A total of 250 subjects were selected and infection was positive in 200 (80%) cases where as 50 (20%) were negative. Same type of study has been done by Shaikh et al. (2005). Oncu et al. (2003) isolated only 3% fungus.

In present study antimicrobial sensitivity of isolated organisms has also been carried out. *E.coli* is highly sensitive with cephalaxin (80%), Ciprofloxacin (CIP) (86%), Ofloxacin (OFL) (88.9%), Amoxil + clavulanic acid (AMC) (77.9%), Cephazolin (CL) (84.5%), Cefuroxime (CXM) (64%) while highly resistant to Amoxicillin (AML) (72%), Neomycin (NEO) (79.50%), Gentamicin (GM) (66.7%) and ceftriaxone (CRO) (75.5%).

In this study the extended spectrum of beta lactamase (ESBL) producing organisms, showed resistance from 2nd and 3rd generation cephalosporin and carbapenum. ESBl production was mostly observed in E.coli 4 cases (66.66%) and Klebsiella species 2 cases (33.33%). Study done by Qadir (2005) also observed ESBl production in E.coli, Klebsiella and Pseudomonas aeruginosa.

CONCLUSION

The results of this study support the use of initial antimicrobial therapy to reduce the spread of infection and other complications. Currently ciprofloxacin is regarded as the drug of choice for the treatment of infection

caused by both gram negative and gram positive bacteria in patients on hemodialysis.

Table No. 1: Distribution of Esbl Producing Isolates

No. of specimens	No. of +ve organisms isolated	% of +ve isolates	No. of +ve organisms of Enterobacteriaceae family	No. of ESBL producing organisms	% of ESBL producing organisms
250	200	80%	175	06	3.42%

Table No. 2: Antimicrobial Sensitivity of Gram Negative Organisms Isolated From Hemodialysis Patients

Micro-organism Susceptibility	**AML 10µg**	**AMC 30µg**	**CZ 30µg**	**CL 30µg**	**CXM 30µg**	**CRO 30µg**	**GM 10µg**	**NEO 30µg**	**CIP 5µg**	**OFL 10µg**
E.coli										
Sensitive (%)	28.00	77.90	80.00	84.50	64.00	24.50	33.30	20.50	86.00	88.90
Resistant (%)	72.00	22.10	20.00	15.50	36.00	75.50	66.70	79.50	14.00	22.10
Klebsiella										
Sensitive (%)	29.50	74.50	75.00	70.50	63.50	66.00	35.00	22.20	88.50	73.50
Resistant (%)	70.50	25.50	25.00	29.50	36.50	34.00	65.00	77.80	11.50	26.50
Pseudomonas										
Sensitive (%)	12.00	35.50	64.50	65.50	62.00	69.00	18.00	22.50	78.50	79.00
Resistant (%)	88.00	64.50	35.50	34.50	38.50	31.00	82.00	77.50	21.50	21.00
Proteus										
Sensitive (%)	8.00	75.00	64.80	69.00	68.22	62.00	9.00	7.00	76.00	80.50
Resistant (%)	92.00	25.00	35.20	31.00	31.88	38.00	91.00	93.00	24.00	19.50

Key: Name with Abbreviation: Amoxicillin (AML), Amoxil + clavulanic acid (AMC), Cephalexin (CZ), Cephazolin (CL), Cefuroxime (CXM), Ceftriaxone (CRO), Gentamicin (GM), Neomycin (NEO), Ciprofloxacin (CIP), Ofloxacin (OFL)

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Original Article

Ductal Variations in the Calot's Triangle Seen on Laparoscopic Cholecystectomy

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ABSTRACT

Objectives: To describe the frequency and pattern of ductal variations seen in the Calot's triangle on laparoscopic cholecystectomy.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted in the Surgical Unit 1, Fauji Foundation Hospital, Rawalpindi from December 13, 2008 to February 22, 2011,

Patients and Methods: 200 patients with a diagnosis of biliary colic, cholelithiasis, acute cholecystitis, empyema gall bladder and mucocele gall bladder were included in this study. Patients with age less than 15 years were excluded. Careful dissection of the Calot's triangle was carried out. The anatomical variations of the cystic duct and other anomalous variations in the region were noted and data analyzed on SPSS 10.

Results: The age range was 19 to 88 years with a mean of 48 years. The majority (88%) of the patients presented with a clinical diagnosis of biliary colic. The cystic duct was of normal size in 88%, short in 7%, and long in 5% of the cases. The cystic duct terminated laterally into the common hepatic duct in 94% of the cases, anteriorly into the common hepatic duct in 5% and posteriorly into the common hepatic duct in 1% of the cases.

Conclusions: Each Calot's triangle differs from the other. Ductal variations are the hallmark of this region and their knowledge is mandatory for a safe laparoscopic cholecystectomy.

Key Words: Cholelithiasis, Cholecystitis, Laparoscopic Cholecystectomy.

INTRODUCTION

The overall prevalence of gallstone disease in industrialized countries appears to be between 10 to 20%[1]. Cholelithiasis is common in Pakistan and Cholecystectomy is one of the commonest operation being performed in hospitals[2]. Laparoscopic cholecystectomy is widely accepted nowadays as the gold standard in the treatment of cholelithiasis[3]. This new technique was initially associated with a significant increase in morbidity, particularly iatrogenic biliary injuries and arterial hemorrhage; perhaps due to the lack of knowledge of the "laparoscopic anatomy" of the Calot's triangle.

The common denominator of bile duct injuries during cholecystectomy is a failure to identify the structures in the Calot's triangle. Anomalous variations of the cystic duct are the hallmark of this region. During skeletonization of the cystic duct, the anterior lying artery may be damaged and blind plunges or injudicious use of diathermy current in this region may cause damage to the common bile duct[4]. In the presence of such variations and superimposed inflammation, dissection of the Calot's triangle is the most important step in open as well as laparoscopic cholecystectomy[5].

Extra-hepatic biliary injuries play a major part in the morbidity and mortality associated with laparoscopic cholecystectomy. Such an injury is very likely in the presence of variant anatomy in the Calot's triangle[6]. This study will help surgeons in identifying the variations in the cystic duct, thus reducing complications like iatrogenic injuries. It will also help decrease the morbidity and mortality associated with laparoscopic cholecystectomy as well as understand how anatomical variations can contribute to complications.

PATIENTS AND METHODS

It is a descriptive study in which the pattern and frequency of vascular and ductal variations in the surgical anatomy of Calot's triangle is described. This study was conducted at the Surgical Unit 1 of Fauji Foundation Hospital, Rawalpindi from December, 2008 to February, 2011. A total of 200 patients were included who underwent laparoscopic cholecystectomy done by 03 consultant laparoscopic surgeons. All these patients were admitted either through emergency or surgical out-patient department with the diagnosis of biliary colic, cholelithiasis, acute cholecystitis, empyema gall bladder and mucocoele of gall bladder. Patients of age less than 15 years or having Hepatitis B or Hepatitis C infection were excluded from the study.

Each patient was evaluated by detailed history and thorough physical examination. Complete Blood Count (CBC), urine analysis, serum urea and creatinine, random blood sugar, liver functions tests (LFTs), hepatitis screening and ultrasound abdomen were done. Selective intra-operative cholangiography was used in those patients who had elevated LFTs or a history of jaundice.

We frequently used nasogastric tube decompression of the stomach. In all our cases, pneumo-peritoneum was created by the open technique (Hasson's method) and four ports (umbilical, epigastric, right hypochondrium and right paracolic) were used. The Calot's triangle was displayed by holding the infundibulum of the gall bladder with grasping forceps. The loose areolar tissue in the Calot's triangle lateral to the cystic lymph node of Lund was dissected with great care. With the help of a Maryland's forceps, small strands of tissue were dissected to skeletonize the cystic duct and cystic artery. The use of diathermy current was minimal during dissection of the Calot's triangle. For minor bleeding in that area, only pressure and packing was successful. The cystic duct was clipped only when the operating surgeon was certain about its entry into the gall bladder. The cystic artery was either clipped or coagulated with diathermy depending upon each surgeon's preference. To measure the length of the cystic duct, the tip of a maryland's forceps was used as a reference which is about 1cm. in length.

Dissection of the Calot's triangle was assigned as easy or difficult by the the operating surgeon. Gall bladder dissection was done by a hook, spatula or scissors with the help of diathermy depending on each surgeon's preference. The gall bladder was extracted through the epigastric or umbilical port with the help of an extractor, either in a glove pouch or without it, again depending on the surgeon's preference.

Data Collection Technique

Informed consent was taken from all patients prior to inclusion in the study. Data collection was done on a pre-designated patient performa. Anatomy of the Calot's triangle was mentioned under the headings of normal and varied anatomy including anomalies of the cystic duct, cystic artery and other anomalies like the duct of Lushka, aberrant Right hepatic duct and Mirrizzi's syndrome. The cystic duct length was measured using the tip of a maryland's forceps and designated as short, medium and long. The number of cystic ducts and their joining point with the common hepatic duct (T Junction) were noted. Other operative findings noted included the type of the gall bladder dissection forceps used and the gall bladder extraction port and technique used.

Data Analysis

The data of 200 male and female patients undergoing laparoscopic cholecystectomy was collected on the pre-designated patient performa and then transferred to the data sheet IV of SPSS 10. This data sheet was then analyzed for median age, mean age, frequency of male and female patients and presentation of symptoms. The frequency calculation for the cystic duct length, difficult dissection and miscellaneous variations was performed with the help of descriptive statistics from this data sheet.

Being a descriptive study, there was no hypothesis designed in our study to assess the probability of error / chance findings.

RESULTS

The age range was from 19 years to 88 years. The median age was 48 years. Our study was based on non-probability / convenient sampling. Only 4 (2%) patients of our study population were male. The majority of the study population was female i.e. 196 (98%) patients. In our study, the weight of the patients ranged from 38 kilograms (kg.) to 100 Kg. The median weight was 65 Kg. The hemoglobin (Hb.) of patients ranged from 9.40 gm/dL to 15.90 gm/dL. The median Hb. was 12.40 gm/dL. The range of patients' white blood cell count (WBC) was from 4.90 x 10^9/L to 17.30 x 10^9/L. The median WBC was 7.90 x 10^9/L. The Alkaline phosphatase (AP) levels ranged from 36 IU/L to 199 IU/L. The median AP was 118 IU/L. The most common clinical diagnosis was biliary colic seen in 176 patients (88%). Acute cholecystitis was seen in 14 patients (7%) while 4 patients (2%) had an empyema gall bladder and 6 patients (3%) had a mucocele of the gall bladder. A nasogastric tube was used in 164 patients (82%).

Conventionally, the dissection in the region of Calot's triangle was assigned as easy and difficult. In 18 patients (9%), the surgeon designated the operation as difficult due to thick adhesions in the Calot's triangle, but was able to dissect the triangle safely. The rest of the cases were designated as easy i.e. 182 patients (91%).

In 66 patients (33%), dissection was done by spatula with diathermy while in 98 patients (49%), hook with diathermy was used. Only in 36 patients (18%), scissors were used for dissection.

In our study, a single cystic duct was found in all 200 cases (100%). We divided the cystic duct length into short (<1cm), normal (1-3cm) and long (>3cm) groups using the tip of a maryland's forceps. The cystic duct was found to be of normal length in 176 patients (88%) (Figure 1). A short cystic duct was found in 14 patients (7%) and a long cystic duct was present in 10 patients (5%). The cystic duct terminated into the common hepatic duct to form the common bile duct (CBD) in all 200 patients (100%). A common termination was

laterally into the common hepatic duct in 188 patients (94%), in 10 patients (5%), the cystic duct terminated anteriorly into the common hepatic duct while in 2 patients (1%), the cystic duct was joining the common hepatic duct in a posterior position (Figure 2).

Figure 1: Variation of Cystic Duct Length.

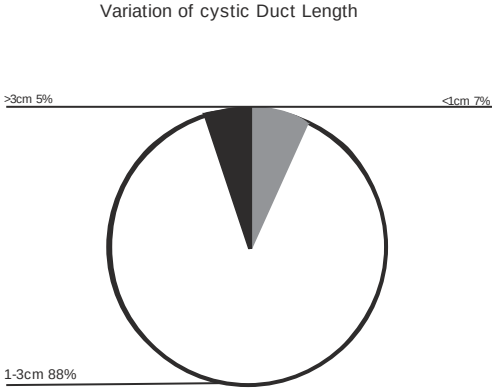
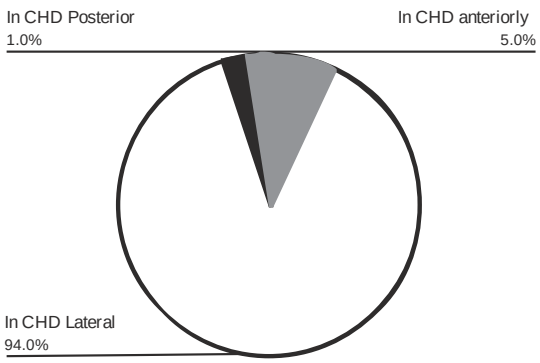


Figure 2: Variation of Cystic Duct Termination.



Complications

4 patients (2%) out of 200 suffered from intra-operative hemorrhage which required conversion to open operation. One patient had hemorrhage from a supra-duodenal vein injury, which was revealed by about 500 ml. of blood in the drain within 20 minutes of completion of laparoscopic cholecystectomy. The patient was operated by open technique and bleeding from a supra duodenal vein was controlled by pressure and ligature of the vein. The second patient had a difficult dissection of the gall bladder from its fossa in the liver due to hepatomegaly and an over hanging left lobe, so the procedure was converted to open cholecystectomy. The other 2 patients had bleeding from the cystic artery which required conversion to open surgery.

DISCUSSION

Laparoscopic cholecystectomy is routinely performed at many hospitals in Pakistan[7]. Muhe performed the first laparoscopic cholecystectomy in 1985[8]. Surgeons have been trying ever since to emphasize the importance of safe dissection in the Calot's triangle. Laparoscopic cholecystectomy mandates great attention to the anatomical dissection of the Calot's triangle in order to accurately identify the cystic artery and cystic duct and any other vascular and biliary structures[9].

Cholelithiasis is a disease of the fourth and fifth decades of life. In our study the age range was 19-88 years. The mean age was 48 years. The age distribution in this study population is the same as that of western population[1]. In our study, the mean weight of patients was 65 kg. The range was from 38 to 100 kg. Our study shows that cholelithiasis occurs mainly in obese patients as described in classical textbooks[10].

In our study, 98% of patients were female. The sampling method of our study was non probability / convenient. Only 4 (2%) male patients presented with cholelithiasis during our study period and were included in the study as part of our inclusion criteria. International data suggests that gallstone disease is 3 to 4 times more common in females than males[11]. A different scenario was reflected by our study population as it was almost exclusively diagnosed in females (98%). However, our hospital mainly treats the families of retired army personnel and the majority of patients are female.

The most common clinical presentation was biliary colic in 88%. Acute cholecystitis was seen in 7%, mucocele in 3% and empyema in 2% cases. In his study, Salman Yousuf Guarya noticed similar results i.e. 476 (86.7%) cases presented with chronic cholecystitis, 63 (11.4%) acute cholecystitis, 6 (1%) mucocele of the gallbladder and 2 (0.4%) had empyema gallbladder[12]. Laparoscopy appears to be a safe and good approach for emergency cholecystectomy in patients with acute cholecystitis[13]. In our study, we noted that the gall bladder contained a single calculus in 38 (19%) patients and multiple calculi in 162 (81%) patients on ultrasonography. Khadim Hussain noted in his study that pre-operative ultrasound in gall stone disease showed a 92% accuracy when its findings were compared with operative findings[14].

In 182 (91%) patients the dissection was easy while it was difficult in 18 (9%) patients keeping in view that patients with complicated gall stones were included in the study. Kwon and colleagues performed laparoscopic cholecystectomy in 440 patients and encountered difficult dissection of the Calot's triangle due to severe adhesions in 10.9% cases[15]. Maudar KK also assessed patients for difficult dissection in the region of the Calot's triangle. Among the difficult cases, they found Mirrizzi's syndrome in 17%, shrunken gall bladder in 32% and a frozen Calot's triangle 51%[16]. A surgeon

performing laparoscopic cholecystectomy can expect a difficult case after every eighth or ninth laparoscopic cholecystectomy. This warrants extra care to avoid mishaps even for experienced surgeons, especially when a variant anatomy is present.

The most common variation was a cystic artery anterior to the cystic duct in 12 (6%) cases. Ayaz and colleagues reported an anterior cystic artery in 15% of cases[4]. This anomaly is dangerous because during skeletonization of the cystic duct, the anterior lying artery may be damaged and blind plunges or injudicious use of diathermy current in this region may cause damage to the common bile duct. The different frequencies of cystic duct position found in our study, corresponds to local and international data.

The literature contains case reports of congenital absence of the cystic duct. Probably the variation is too rare. We were unable to find such a variation.

During our procedure, we divided the cystic duct length into short cystic duct (<1cm), normal cystic duct (1-3cm) and long cystic duct (>3cm). By conventional method, the length of the proximal end of a maryland's forceps is taken as 1cm. In our study, 176 (88%) cases had a normal cystic duct, 10 (5%) cases had a long cystic duct and 14 (7%) cases had short cystic duct. The length of the cystic duct in the Calot's triangle is important because the "classical" biliary injury usually involves misidentification of the common bile duct as the cystic duct. Strasberg and colleagues described the "hidden cystic duct syndrome" i.e. the cystic duct may be hidden in inflammatory tissue behind the common bile duct and a false infundibulum may be seen, connecting the common bile duct and gallbladder. It is here that the common bile duct is mistaken as the cystic duct[17, 18].

The study performed by Francouer further highlights the importance of the length of the cystic duct. A response to a questionnaire from 114 Laparoscopic Surgeons is reported in his study. It cites inflammation and short / anomalous cystic ducts as the most responsible factors contributing to injury[19]. This misperception can occur if the cystic duct is absent or of very short length. In our study, we found that the cystic duct was short in 7% of patients and in these cases, superimposed inflammation gave the impression of a false infundibulum and a hidden cystic duct syndrome. The CBD is at risk of injury in such variations of length[18].

In our 200 (100%) cases, we noticed a single cystic duct. In 188 (94%) cases, the cystic duct was terminating laterally into the common hepatic duct. The common variation was the termination of the cystic duct into the common hepatic duct anteriorly in 10 (5%) cases. In 2 (1%) cases, we found the cystic duct terminating posteriorly into the common hepatic duct. In a study by Fatima, she noticed an original pattern described in textbooks i.e. union of the cystic duct on the lateral side of the common hepatic duct in only 32% cases[20]. Such may be the variation in the anatomy of the T junction.

In this study, we performed gall bladder dissection with the help of spatula, hook or scissors. In 66 (33%) cases, dissection was done by a spatula with diathermy. In 98 (49%) cases, hook with diathermy was used while in 36 (18%) cases, scissors were used for dissection.

4 patients (2%) out of 200 suffered from intra-operative complications. None of these were related to major extra-hepatic hepatic duct or surrounding structures. One patient had hemorrhage from a supra-duodenal vein injury, which required conversion to open technique and bleeding control by pressure and ligature. The second patient had a difficult dissection of the gall bladder from the liver bed due to hepatomegaly and an overhanging left lobe of liver, so the procedure was converted to open cholecystectomy. The other 2 patients had bleeding from the cystic artery which required conversion to open surgery. Khan in his study noticed a conversion rate of 6.4%[21]. The morbidity encountered in our study is comparable to local and international data and is in the acceptable range. There was no mortality in this series. More emphasis is however needed to properly train young surgeons in the field of laparoscopic surgery[22].

CONCLUSIONS

In the dissection of the Calot's triangle for routine laparoscopic cholecystectomy, the concept of the so called normal / abnormal or anomalous anatomy is difficult to state. Certainly, the anatomy of Calot's triangle is a "VARIANT ANATOMY" and after doing this original study and an extensive review of pertinent literature, this is how we state it.

Just like their genes, faces and finger prints, Calot's triangles of humans differ from each other. It is almost impossible to find two congruent Calot's triangles. The knowledge of a variant anatomy in the Calot's triangle is the key for dissection. Surgical trainees should be taught this principle for doing a safe cholecystectomy.

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Original Article

Etiology of Primary Amenorrhoea: A study of 50 cases

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ABSTRACT

Background: Amenorrhoea is one of the commonest reasons for referral of female patients to a gynaecology clinic. It is subdivided into primary and secondary. The etiology of primary amenorrhoea is complex.

Objective: The aim of this study was to determine the etiological factors of primary amenorrhoea and to find out the mean age at first presentation.

Design of Study: Descriptive Study.

Place and Duration of Study: This Study was conducted in the department of Obstetrics and Gynaecology Foundation University Medical College Fauji Foundation Hospital Rawalpindi, from 1st January 2005 to 31st December 2007.

Materials and Methods: 50 girls who reported to gynae outpatient department with the complaint of primary amenorrhoea were included in the study after informed consent. Detailed history, clinical examination and investigations (transabdominal ultrasonography, hormonal profile including serum FSH, LH & prolactin, karyotyping) were recorded in proformas for analysis.

Results: A total of 50 girls reported to gynae OPD with complaints of primary amenorrhoea over a period of 24 months with the mean age of 18.5 years at initial presentation. Almost half of the girls (48%) with normal secondary sexual characteristics had anatomical defects, Rokitansky's syndrome being the commonest, while those with absent secondary sexual characteristics had constitutional delay as the commonest cause.

Conclusion: Mean age at first presentation is late. Anatomical causes are the commonest. Turner's syndrome is relatively uncommon in our patients.

Key Words: Primary Amenorrhoea, Transabdominal Ultrasonography, Hormonal Profile (FSH, LH, Prolactin), karyotyping

INTRODUCTION

Amenorrhoea is one of the commonest reasons for referral of female patients to a gynaecology clinic. It is subdivided into primary and secondary. Primary amenorrhoea is defined as failure of onset of menstruation by the age of 14 years in girls without secondary sexual characteristics (SSC) or by the age of 16 in girls with normal SSC [1, 2]. It is a rare disorder and the quoted international incidence is 0.3 %.[3]. The etiology of primary amenorrhoea is complex. At the initial visit of the patient thorough clinical evaluation and endocrine tests can help to established the diagnosis in most cases [4, 5]. In addition assessment of pubertal development is an essential part [6]. A careful evaluation is necessary not only to treat the patient but also for the support and counselling of the patient and the family.

The commonest cause is physiological i.e. constitutional delay. However this diagnosis should only be made after exclusion of other pathological causes [7]. The most common pathological cause associated with normal SSC is an anatomical abnormality of vagina (1 in 4000 women)[1] and that associated with absent secondary SSC are Turner's syndrome (1 in 2000-3000 girls), hypothalamic-pituitary dysfunction and chronic systemic illnesses [8]. Overall it is estimated that endocrine disorders account for approximately 40% and developmental defects for 60% of the cases of primary amenorrhoea[9]. A systematic approach can help to determine the common causes of primary amenorrhoea and also helps to reach the diagnosis in a cost effective manner.

We conducted this study to look for the common causes of primary amenorrhoea in our setup and to know the mean age at first presentation as this problem occurs at such a delicate, sensitive age that if not handled properly can lead to permanent physical as well as psychological disability.

MATERIALS AND METHODS

This study was conducted over a period of two years from 1st January 2005 to 31st December 2007 in the department of obstetrics and Gynaecology Foundation University Medical College Fauji Foundation Hospital Rawalpindi. All patients who reported to gynae clinic with complaint of primary amenorrhoea were included in the study.

At the initial visit of the patient a detailed history especially regarding growth and development , family history and age of menarche in siblings was taken. This was followed by a thorough physical examination

including general physical examination with special reference to weight, height and secondary sexual characteristics (development of breast, pubic and axillary hair and growth spurt) and abdominopelvic examination for the presence of abdominal gonads, any mass and the development of external genitalia. The next step was to perform transabdominal ultrasonography (TAS) to look for the presence or absence of uterus and gonads followed by hormonal profile (serum FSH, LH and prolactin) and karyotyping. All findings were entered in a proforma for detailed analysis.

RESULTS

A total of 50 girls reported to gynae OPD with complaint of primary amenorrhoea over a period of 24 months with the mean age of 18.5 years at initial presentation (Table No. I). The characteristics of our study population revealed that 96% were married, family history was positive in 10% and majority belonged to lower socioeconomic class (Table No.2).
Regarding the etiological factors almost half of the girls (48%) with normal SSC had anatomical defects (Fig I), Rokitansky's syndrome being the commonest (Fig II) while those with absent SSC had constitutional delay as the commonest cause (Fig III).

Table I: Mean age, weight & height (n=50)

	Mean	Range
Age (yrs)	18.5	12-31
Weight (Kg)	51.6	36-65
Height (cm)	157.2	147.3-167.6

Table II: Characteristics of study population (n=50)

Characteristics		Number	percentage
Marital Status	Married	1	2
	Unmarried	49	98
Education	Students	40	80
	Uneducated	10	20
Family history	Positive	5	10
	Negative	45	90
Socioeconomic Status	Lower Class	34	68
	Middle Class	15	30
	Upper Class	1	2

DISCUSSION

Primary amenorrhoea is a rare disease[3]. A total of 40945 patients attended gynae clinic in two years and 50 patients (1.2%) had primary amenorrhoea. The reason for high frequency is that our hospital is a tertiary care referral hospital and many patients are referred to us from periphery for specialist care. A local study also quoted a high frequency 0.75% for the same reason[9].

Figure No.1: Distribution according to SSC (n=50).

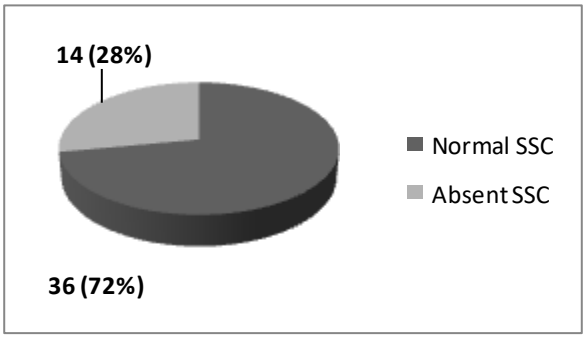


Figure No.2: Anatomical defects (n=50)

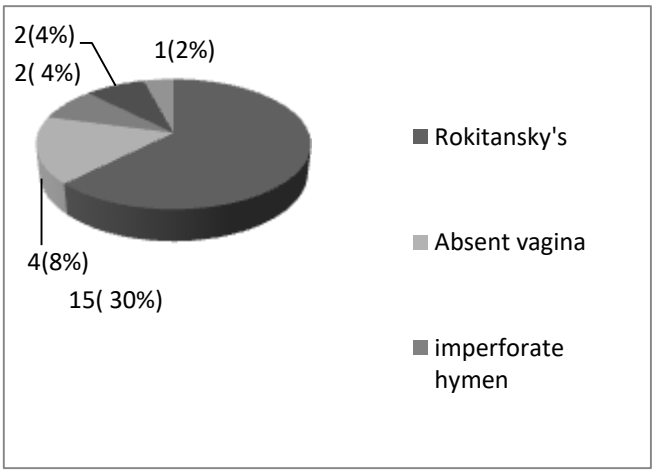
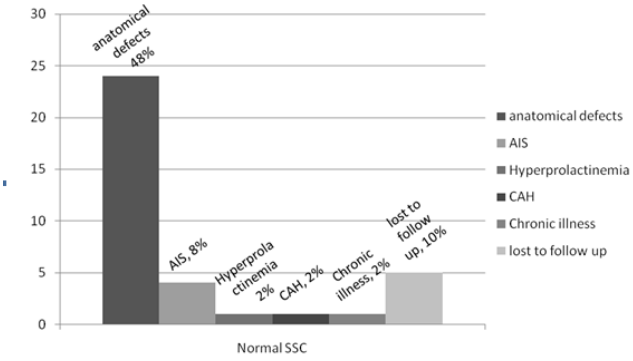


Figure No.3: Etiology of Primary Amenorrhoea (Normal SSC) (n=50)



Causes of primary amenorrhoea should be evaluated in the context of the presence or absence of SSC[10]. In our study population 36 (72%) had normal SSC and 14 (28%) had absent SSC. Our findings were favoured by a local study in which around 70% of the patients had developed SSC[11]. Our results showed that mean age at first presentation was late (18.5 years). This is probably

due to two reasons. Firstly these young girls belong to poor families and are unable to reach the hospital due to lack of transport. Secondly they are attended at first hand by quacks and general practitioners and are often misdiagnosed. An age range between 15-25 years at first presentation was also observed in different studies[11].

Characteristics of our patients showed that majority were unmarried and belonged to lower socioeconomic class. This is due to the reason that primary amenorrhoea is a disease seen in adolescent age group when mostly girls are unmarried and the reason for majority being from lower socioeconomic class is that our hospital is entitled for the families of retired army servicemen who have worked in lower ranks up to the level of subedars and have low income after retirement.

Our main objective was to determine the etiology of primary amenorrhoea. The most common pathological cause associated with normal SSC is an anatomical abnormality of vagina (1 in 4000) varying from the more common imperforate hymen to relatively rare absent vagina[1, 8]. Our results also confirmed that girls who had normal SSC, anatomical abnormality was the commonest (48%) i.e. almost half of our study group. This was followed by androgen insensitivity syndrome (AIS) seen in 8%, congenital adrenal hyperplasia, chronic medical illness and hyperprolactinemia in 2% each. Asifa and Shazia[12] also quoted a very high incidence of anatomical defects 46.15% and even much higher (61.1%) in another local study[13]. However an Indian study reported an incidence of 37.5% in their population[14]. Amongst the anatomical causes Rokitansky's syndrome (the congenital absence of Mullarian ducts) is said to be responsible for 15 % of patients with primary amenorrhoea[15]. The etiology involves activation of antimullerian hormone causing malformation of female genital tract[16]. In contrast our study showed a much higher frequency (30%). Few other studies have also quoted a much less frequency (1in 5000)[17].

A patient with primary amenorrhoea and an XY karyotype who has breast development and minimal or no pubic and axillary hair, the diagnosis is AIS. If testes are present they must be removed because of high risk of malignant potential[18]. AIS was present in 8% of our patients that is exactly the same as in a study conducted in Hong Kong[19]. However, Shazia[13] quoted a frequency of 11% and a Mexican study showed 10.7% of their patients with AIS[20].

Imperforate hymen and congenital uterine abnormalities were less commonly seen in our patients (4% each). This does not correlate with other studies that reported a more common frequency of imperforate hymen[11].

Chronic debilitating diseases e.g. uncontrolled diabetes, malignancy, end-stage kidney diseases may lead to anovulation and amenorrhoea[21]. In our study one patient has uncontrolled diabetes and presented with amenorrhoea. Other rare causes were congenital adrenal hyperplasia and hyperprolactinemia.

The other group of girls having absent SSC had constitutional delay as the commonest cause (14%). This observation is favoured by Folch and Seldmeyer[15, 16]. Ovarian failure, a rare cause of primary amenorrhoea could be due to resistant ovary syndrome[22]. It is seen in 6% of our study population in contrast to study of Noshaba and Razia who failed to find ovarian failure in their patients[9]. However few cases of ovarian failure have been reported in other studies[23].

Turner's syndrome (45 XO) is the most common form of female gonadal dysgenesis. Characteristic physical findings are webbing of the neck, widely spaced nipples and short stature. Mosaicism occurs in 25% of patients with Turner's syndrome[24].

In our study the frequency of Turner's syndrome was low (4%) and same was the frequency of hypogonadotrophic hypogonadism. However it was high in the study of Naushaba and Asifa Ghazi (10.52% and 30.78% respectively)[9, 12].

CONCLUSION

We concluded that mean age at first presentation was late in our patients and anatomical cause was the commonest cause of primary amenorrhoea.

The diagnosis is traumatic for both girls and their parents because there is fear of loss of fertility, feminity and self esteem. These young girls are in a true emotional crisis about being different from friends and family. So a systematic approach is essential to reach a correct diagnosis and counselling in a sympathetic way is an essential component of management.

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Original Article

Management of 30 cases of Malignent Skin Lesions at the lower eyelid and cheek with cervicofacial flaps

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ABSTRACT

Object: To assess suitability of this flap with respect to defects in this area.
Design: Observation study.
Place and duration: Department of Plastic Surgery and Burns Bolan Medical College & Complex Hospital Quetta, from January 2003 to December 2009.
Patient and Methods: 30 cases were operated with reconstruction using cervicofacial flaps. Patients were selected through Out Patient Department. Follow up 3 & 6 months.
Results: Flaps survival was 100 % with partial flaps necrosis at tip of the flaps in 4 cases, with large defects recurrence was observed in five cases.
Conclusion: Procedure was found to be suitable with regards to large defect i.e (4 cm to 6 cm).
Keywords: Skin Tumors & cheek defects, cervicofacial flaps.

INTRODUCTION

Skin cancer has become common in our part of the world as it used to be common in other parts of the world such as United States, Europe and Australia .The incidence is more common in fair skinned people than in coloured people.

The incidence is directly related to ultra violet exposure. It is that highest in sunny climates people working out door and people not covering their parts of body with clothings. The ultra violet Radiation causes electron excitation in absorbing atoms and molecules inducing damaging chemical reaction which results in damage to DNA resulting in cell death and new plastic transformation.

These lesions have good prognosus if treated at an earlier stage, other wise they are fatal and deforming.

We working in the Department of Plastic Surgery at Quetta receive a lot of patients from far flang areas including Balochistan, parts of Sindh, and Punjab .The areas of Afghanistan & Iran adjoining the border also approach Quetta for treatment. The people living in these areas are mostly illiterate, poor, and basic health facilities are scarce. Further more, great distances and lack of infrastructure facilities have made the conditions worse. The above factors make it very difficult for the masses to seek advice and treatment, regarding their health problems.

Most of our patients approach at a stage where disease is advanced. And in a few patients disease has reached to a stage where surgical intervention is difficult and other measures are adopted.

Our department receives a great number of skin malignancies involving all parts of the body specially expose parts i.e Face, specially cheek, canthal areas, nose and lips, are the areas receiving the bulk of sun light, resulting in increased incidence of malignancies.

Following Factors are related with the incidence of these malignancies:

Ultra violet Radiation:

The incidence of skin cancer is directly related to ultra violet radiation it is highest in sunny climates, in people with light complexion. Here the radiation induced chemical change in DNA is responsible for cell death and new plastic transformation. The effects of ultra violet radiation are reduced by the presence of hair, thick stratum corneum and melanin. The thinning and the holes in the ozone layer has increased the hazards associated with ultra violet exposure resulting in great increase in number of skin malignancies.

Ionizing Radiation:

Ionizing radiation was also associated with skin cancer which include X-Rays, Gamma Rays and particulate radiation i.e electrons, protons, neutrons and heavy nuclei.

Chemical Carcinogens:

Chemical carcinogens such as Arsenic psoralens nitrogen mustard are also related. Carcinogenesis occurs through bio-chemical interaction i.e covalent bonding of carcinogen with cellular macro molecules.

Genetic Determinants:

They play a major role in the pathogensis.

Xeroderma pigmentosum:

An inherited condition . Xeroderma pigmentosum, is characterized by ultra violet induced DNA damage resulting in multiple epithliomas with subsequent malignant change.

Albinism:

With hypopigmentation of skin, hair and eyes. There is increased risk of Squamous cell and basal cell carcinoma.

Among the skin cancer the three main types, most prevalent are

(i) Basal Cell Carcinoma
(ii) Squamous Cell Carcinoma
(iii) Maligment Melanoma.

PATIENTS AND METHODS

Most of the patients were received in the out door department of Plastic Surgery and Burns. Patients were admitted to the Department of Plastic Surgery and Burns at Bolan Medical Complex Hospital Quetta from April 2003 till to December 2009. Patients were classified according to the age, sex, occupation, presentation and site of the disease and type of tumor .Diagnosis was made on the basis of clinical presentation and histopathology.

RESULTS

Study consist of thirty cases operated from Jan 2003 to Dec 2009 in almost all the cases the defect was located at the cheek either involving lower eyelid or the inner canthal area.

All the defects were reconstructed using cervicofacial flap. This procedure involves extensive dissection of the cheek preauricular & retroaurcular area and the neck and extending medially downwards to the chin, for flap advancement .This flap is vascularized by the anterior perforators of the internal mamary artery .It may cover the entire aesthetic unit of the cheek.

We observed, all the flaps survived very nicely except partial necrosis at the tip of the flaps. Which work later on healed well. The entire specimen were sent for histopathology. Cases with positive margins were referred for radiotherapy. Recurrence was observed in five cases which were excised and managed accordingly.

DISCUSSION

Aesthetic units of the cheek are the topographic zones of the cheek, sub orbital and preaudicular and bucomandbular area. Although small defects in this area was reconstructed using small local flaps, as the laxity and vascularity of this region enables closure of defects.

But most of the patients were presented at an advanced stage where growth has attained a large size where local flaps could not achieve the desired result in these cases because in the advance case the tissue requirement was greater. This technique proved to be adequate with superior aestheatic results. In most of the cases some degree of ectropion was present which seemed to be unevitable due to tumor invasion of the lower eye lid which was partially or completely excised. The remenient conjectiva was undermined & stitched on to the advancement cheek flap.

In a few cases the lower lid ectropion was partially corrected with free graft.

CONCLUSION

We have been using free grafts from local cheek flaps and cervicofacial flaps with regards to defects on the cheek , lower eyelid and their inner canthal area. We found cervicofacial flap repair as the most adequate aesthetically with least donor area morbidity, providing coverage in large defects.

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Original Article

Histopathological Hepatoprotective Effects by Echinops Echinatus A Plant from Cholistan Desert

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ABSTRACT

Objective of study: Aerial parts of Echinops Echinotus (EE) were subjected to in vivo histological hepatoprotective study in order to validate its traditional use in hepatobiliary disorders, by native people of Cholistan desert, Pakistan.
Design of Study: Experimental study.
Place of study: The study was conducted at PCR lab Multan.
Materials and Methods: The animals were randomly divided into three groups, containing 10 rabbits in each group. Histological hepatoprotective effects of pre-treatment with aerial parts (ethanolic extract) of EE (500 and 750 mg/kg/day PO for 7 days) against CCl_4 (0.75 ml/kg, S/C) intoxicated rabbits were evaluated by liver histological observations. Silymarin (100 mg/kg/day PO for 7 days) was used as a standard hepatoprotective drug.
Results: CCl_4 intoxicated group had significant histological changes (marked fatty changes etc.) as compared to normal control group. However, EE extract produced significant histological hepatoprotective changes.
Conclusion: Therefore, the outcome of present study supports the traditional behaviour on hepatoprotective effects of Echinops Echinatus (aerial parts).
Key words: Ethinops Echinatus, Hepatoprotective.

INTRODUCTION

Cholistan desert is present on the eastern side of Punjab Province (Pakistan)[1]. The majority of plants grow in desert have therapeutic properties and native people utilize these plants to treat various diseases[2].

Echinops Echinatus commonly known as Kandesi Bhattar, Ont Katara is an herbaceons plant, widely distributed in desert regions of Pakistan. It root, leaves, fruit and bark are most commonly used parts[3]. In folk medicine, its root powder with honey is given as general tonic. Herb is used as liver stimulant[4].

Native people of cholistan desert use this plant in hepatobiliary disorders. However to best of our knowledge, no previous work has been published on histological protective on liver by this plant.

Present study was aimed to evaluate the histological hepatoprotective effects of EE against CCl_4 induced hepatotoxicity.

MATERIAL AND METHODS

Ethanol, CCl_4, formalin, xylene, paraffin wax, eosin, hematotoxylin and Canada balsam, all chemical of analytical grade were used.

Echinops echinatus was collected from cholistan desert and authenticated by toxanomist. Plant material was dried under shade, cut into small pieces and then subjected for grinding. For convenient administration, the dry extract was encapsulated after weighing.

Healthy rabbits of either sex (local bread) weighing from 1.5-2 kg were purchased from local market. The animals were maintained at standard housing conditions.

Hepatotoxicity was induced by subcutaneously by CCl_4 at a dose 0.75 ml/kg body weight. The animals were randomly divided into three groups, containing 10 rabbits in each. CCl_4 was injected 30 minutes after drug administration.

Animals were sacrificed and histological assessment was done according to standard methods[5]. The pathological changes of fatty liver and degenerations of liver cells were graded as under:-

Group-0 (normal):- Normal liver morphology; hepatocytes with round nucleus centrally with homogenous cytoplasm, flat endothelial cells around central vein and sinusoid.

Group-+1 (mild degree):- 1-2 hepatocyte rows around central vein showed; hepatic cell degeneration along with necrosis (loss of nucleus), less injury of endothelial cells around central vein, less fat vacuoles in hepatocytes.

Grade-+2 (moderate degree):- Some hepatocyte rows around central veins showed: swelling, intracytoplasmic vascular degeneration in centrilobular, midsonal and periportal aras endothelial cells around central areas endothelial cells around central vein more damage than level +1 more fat vacuoles in hepatocytes than level +1.

Grade-+3 (severe degree):- 3-4 hepatocyte rows around central vein demonstrated; hepatocyte degeneration and necrosis, degeneration cells including centrilobular, midzonal and periportal areas (diffuse intracytoplasic vascular degeneration), endothelial lining of central vein showed more cell damage, increased fat vacuoles in hepatocytes than level +2, marked focal necrosis.

The results were presented as mean + standard error of means (SEM). Multiple comparisons were performed by student's t-test. Difference were considered statistically significant when $P < 0.05$.

RESULTS

Histopathological changes after 24 hours of CCl_4 induced liver injury included fatty degeneration, hydropic degeneration, vacuole generation, microvascular steatosis and inflammatory cell infiltration. Administration of EE extract significantly preserved normal hepatocellular architecture from damaging effects of CCl_4 as compared silymasin.

DISCUSSION

According to phychochemical analysis, EE contains alkaloids, echinopsine, echinopsidine and echinozolinone etc. many flavonoids liked apigenin, echinacin and triterpenoids like tarazasterol, luperol, tannins, sugars, amino acids, phenols and steroids[6]. The flavonoids are well reputed for their anti-oxidant, free radical scavenges and anti-lipoperoxidation by scavenging reactive oxygen species[8]. Tannins and lignans are also well renowned for their hepatoprotective effects[9]. Moreover, alkaloids[10] and triterpenoids[11] also have hepatoprotective activity. So it is reasonable to think that the observed protective effects of EE extract might be due to the presence of these polyphenolic compounds (flavonoids, quercitin etc.), alkaloids, tannins, saponins and steroid among other plant constituents. Moreover, phenolic compounds amongst many other constituents have been shown to possess hepatoprotective and calcium antagonist activities and the presence of such constituents in extract, may be responsible activities observed in this study.

It is reported that the mice knocked out of CYP2E1 gene show resistance against CCl_4, induced hepatotoxicity and the level of reactive metabolites can be reduced by inhibition of CYP2E1 gene expression, consequently tissue injury is reduced[12]. In recent years, there has been an active search for the development of CYP_{450} inhibitors from natural products that may have therapeutic potential in prevention of liver damage. Tritepene acids, oleanolic acid and ursolic acid inhibit CYP_{450}[12]. So, the hepato-protective action of EE extract may be due to the presence of some of the above mentioned compounds which cause down regulation of CYP2E1 gene expression but it must be confirmed after a detail phytochemical analysis of the plant.

To be brief, the possible hepatoprotective mechanism of EE aerial parts ethanolic extract of CCl_4 induced liver injuries may be through one of actions prevention of process of lipid oxidation, free radical scavengers or down regulation of CYP2E1 gene expression.

CONCLUSION

It is concluded that study provides scientific root for the conventional use of Echinops Echinatus in hepatobiliary diseases in eastern system of medicine. Further studies should be carried out to determine the therapeutic index and exact mechanism of hepatoprotection offered by the plant.

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Original Article

Comparison of Efficacy and Tolerability Between Sertraline and Fluoxetine in Patients With Major

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ABSTRACT

Objective: Aim of this study was to compare the efficacy and tolerability between Sertraline and Fluoxetine to determine suitable treatment of major depression in Pakistani population.

Place and Duration: This study was conducted in the outpatients department of psychiatry, Jinnah Postgraduate Medical Centre, Karachi. The duration of the study was 24 weeks conducted from January – December 2008.

Materials and Methods: 100 male and female patients between 18 to 65 years of age with a diagnosis of major depressive disorder were selected. Two groups A1 and A2 were made of 50 patients each. Group A1 received Tab Sertraline while Group A2 received Cap Fluoxetine daily for 24 weeks after going through screening tests and diagnostic evaluation. Efficacy was evaluated by using 21 item Hamilton Depression Rating Scale (HDRS) and 20 item Self Reporting Questionnaire (SRQ). The patients were asked to attend the OPD every 15 days. Side effects and compliance of the patients was noted at each visit.

Results: The results showed that both groups showed significant improvement in depression from week 0 to week 24 with minimal adverse effects. Compliance of the patients in both groups was good. Although HDRS and SRQ scores were significantly reduced in both groups, it was noted that Tab Sertraline improved the symptoms earlier than Cap Fluoxetine.

Conclusion: It can be concluded that both sertraline and fluoxetine are efficacious in major depression causing few adverse effects but because sertraline improves symptoms earlier and it is cost effective it may be preferred to fluoxetine.

Key Words: Major depression, Hamilton Depression Rating Scale, Self Reporting Questionnaire, Bradford Somatic Inventory.

INTRODUCTION

Depression is common is all regions of the world. It constitutes substantial proportion of the global burden of disease and is projected to form the second most common cause of disability by 2020[1,2].

In Pakistan the magnitude of mental illness is serious. The prevalence of depressive disorder is the highest. Besides other social evils, these mental morbidities are responsible for the high suicide rate as noted recently[1,3].

Social adversity and relationship problems are major risk factor for depressive disorder in Pakistan. The prevalence of depression in Pakistan is 33% that is every third Pakistani is expected to be suffering from depression. Rates for depressive disorder are reported to be higher in women than men that is consistent with the estimates from western countries[1,4].

Depression is the eighth leading cause of death in the United States. Fortunately, about 80% to 90% of depressed patients can be treated successfully. About 65% of patients ultimately respond to antidepressant drug therapy and completely recover[5].

Although very common, depression is often ignored, misdiagnosed and left untreated. Such inattention can be life-threatening: major depression in particular has a high suicide rate[6].

Fortunately, there are a number of efficacious medications to choose from when treating a depressed patient. The most significant class of antidepressants marketed in recent years is the selective serotonin reuptake inhibitors (SSRIs). Primary use for the SSRIs is unipolar major depression. Among the SSRIs, there are more similarities than differences. Nevertheless, there are differences between SSRIs that could be clinically significant [7].

The objective of this study is to describe the significant differences in efficacy and tolerability between two most commonly used SSRIs that are fluoxetine (Prozac) and sertraline (Zoloft) and to identify their role in treatment of major depression. SSRIs are potent inhibitors of serotonin reuptake. Three neurotransmitter deficiency syndromes are associated with depressed mood. These include a serotonin, a norepinephrine, and a dopamine deficiency syndrome. Fluoxetine has effects on serotonin and norepinephrine while sertraline has effects on serotonin and dopamine[7].

Fluoxetine & Sertraline

These drugs work by preventing the reuptake of neurotransmitter, serotonin, by nerve cells after it has been released. Since uptake is an important mechanism for removing released neurotransmitters and terminating their actions on adjacent nerves, the reduced uptake causes increased free serotonin that stimulates nerve cells in the brain. In USA alone fluoxetine is the third most prescribed antidepressant. Sertraline in 2007, was the most prescribed antidepressant in US[8].

Onset of Activity: the mood-elevating effect of antidepressant medication usually begins about 1 to 2 weeks after initiation of treatment. The clinical rule of thumb is that a patient must be treated with an adequate dosage for at least 6 weeks before the clinician considers changing the treatment[5].

MATERIALS AND METHODS

This study was conducted in the outpatients departments at the Department of Psychiatry, Jinnah Post Graduate Medical Centre, Karachi and Department of Psychiatry, PNS Shifa Hospital, Karachi in patients diagnosed with major depressive disorder.

The proposed study was spread over a period of 24 weeks. All the patients fulfilling the following inclusion and exclusion criteria were included in the study:

Inclusion Criteria

1) Male and female outpatients, 18 to 65 years of age.
2) The patients had to meet the DSM-IV criteria for major depressive disorder, single episode or recurrent.

Exclusion Criteria

1) Failure to respond to more than one adequate trial of an approved antidepressant medication for the current episode of depression.
2) Presence of a primary psychiatric illness other than major depression.
3) Pregnant and breast-feeding women.
4) Previous head injury.

Subject Recruitment:

Despite extensive research to find a diagnostic test, the diagnosis of depression remains clinical. The criteria for the diagnosis of major depression are the core signs and symptoms. A clinician's index of suspicion about the diagnosis of depression should be raised if a patient presents with a chief complaint of fatigue, pain, sleep disturbances, anxiety, irritability, or gastrointestinal problems[5].

100 patients were enrolled in this study, 50 patients received tablet sertraline 50 -200 mg daily (group A1), while 50 patients received capsule fluoxetine 20 -80 mg daily (group A2). Both these groups were compared for efficacy, compliance and tolerability after going through screening tests and diagnostic evaluation by Psychiatrists.

All subjects gave written consent before induction in the study[9].

All subjects were at least 18 years of age, conversant in Urdu, and willing to be available for participation in the 24-week study[10].

On enrolment, each patient received complete physical examination, and laboratory tests were also performed.

All registered patients were advised to attend the respective OPDs every 2 weeks until the end of this study.

Psychiatric diagnoses based on DSM-IV criteria were determined by a consensus of at least two psychiatrists using the Structured Clinical Interview for DSM IV [9,10,11].

Evaluation of Subjects:

Psychiatrists have developed a variety of ways to rate how a person is feeling more objectively using psychiatric "RATING SCALES".

Measures used for the initial evaluation of subjects included;

a. Self-Reporting Health Questionnaire (SRQ) [12,13].
b. Bradford Somatic Inventory (BSI)[14,15].
c. Hamilton Depression Rating Scale (16),(17),(18).

Efficacy was evaluated by using the 21 item version of the Hamilton depression scale (HDRS) and 20 item Self Reporting Questionnaire (SRQ).

Hamilton Depression Rating Scale (HDRS) has been the gold standard for the assessment of depression for more than 40 years.

Unlike other depression measures, the HDRS was developed in a medical setting and, for more than 30 years, used concurrently with antidepressant medication to evaluate treatment response. The HDRS has retained this function and is now the most commonly used measure of depression[16,18].

The total HDRS score provides an indication of the level of a patient's depression and over time, provides a valuable guide to our patient's progress.

In general, the higher the total score, the more severe is the depression.

HDRS Score: Level of depression:

10 - 13 Mild

13 – 17 Mild to Moderate

> 17 Moderate to severe

The patients should be assessed at 2 weekly intervals following the initial assessment.

SRQ & BSI

Both SRQ and BSI are effective screening instruments in detection of probable psychiatric cases particularly in case of women. Both the instruments use a simple Yes/No format, which has been found to be easier to comprehend by our population as compared to more complicated response scales.

We have used SRQ scale for efficacy at the beginning and at the end of therapy. SRQ is a 20 item scale with optimal threshold score Males - ≤ 4, Females - ≤ 8.
Bradford Somatic Inventory (BSI) is a 44 item scale with threshold score 25/26 and was used at the beginning of the study.
Subjects had to have normal physical examination and laboratory results, including a complete blood count with Hb%, ESR, Blood sugar (R), AST, ALT. All laboratory tests were repeated at the end of the study period.
Medication compliance was documented at each visit by a count of returned blister packs.
Safety was assessed by physical examination, clinical laboratory tests at screening and at endpoint. At each visit, patients' vital signs were recorded. Subjects were asked about adverse events at each visit and a Utvalg for Kliniske Undersogelser (UKU) side effect scale was used. Adverse effects were divided into psychic adverse effects, neurological adverse effects, autonomic adverse effects and other adverse effects[19].

RESULTS

Statistical comparison was performed by using chi-square for qualitative variables and student t-test, or analysis of variance (ANOVA) for quantitative variables according to treatment within Sertraline and Fluoxetine. In all statistical analysis only p-value <0.05 was considered significant.

Subjects
Out of 100 patients 18% were male (10% in A1 and 8% in A2) while 82% were female (40% in A1 and 42% in A2). Mean age in group A1 was 42.2 years while in group A2 it was 40.2 years. Laboratory tests like BMI, Hemoglobin, ESR, RBS, AST and ALT were performed at the initial induction and then at the end of the 24 week study period. It was seen that between wk 0 and wk 24 no statistically significant difference was noted in these tests except for AST and ALT that were increased significantly from wk-0 to wk-24 ($p<0.05$) (Table No. I).
Mean scoring level of depression according to HDRS was 24 with 22.2 in A1 group (Sertraline group) and 25.8 in A2 group (Fluoxetine group). According to SRQ and BSI the mean levels are 9.4 (9.2 for A1 and 9.7 for A2) and 21.7 (21.4 in A1 and 22.1 in A2) respectively (Table No.2).
At wk 0 the number of patients was 50 in each group that was reduced to 46 in group A1 and 47 in group A2. The relative change from baseline on the HDRS - 21 score was calculated. The responder rate was defined as a reduction of at least 50% on the HDRS - 21 score. Remission was defined as a reduction in HDRS - 21 to 9 or less. After treatment at wk 24 group A1 showed highly significant improvement in HDRS scores, so was the case with group A2 that also showed highly significant improvement at the end of the study period with mean values reducing from 22.2 in Group A1 to 10.7 and in Group A2 from 25.8 to 14.1 with p-value of 0.001 (Table No.3 & 5).
The tolerability and adverse effects were recorded and divided into psychic adverse effects, neurological adverse effects, autonomic adverse effects and other/misc adverse effects. All adverse effects were noted starting from wk 2 and then subsequently every 2 weeks until the end of the study period at 24th week (Table No.6).

Table No. I: Baseline parameters of unipolar depression according to treatment groups (Sertraline A1 vs Fluoxetine A2)

Parameters		SSRIs (n=100)			P-Value
		Overall all (n=100)	Group A1 (n=50)	Group A2 (n=50)	Group A1 vs. A2
Gender	Male	18	10 (20%)	8 (16%)	0.603
	Female	82	40 (80%)	42 (84%)	
Age in years	Mean ± S.D	41.2 ± 9.0	42.2 ± 9.7	40.2 ± 8.4	0.278
BMI	Mean ± S.D	26.9 ± 3.6	27.2 ± 2.9	26.4 ± 2.7	0.165
Hemoglobin	Mean ± S.D	11.4 ± 1.5	11.9 ± 1.6	10.8 ± 1.3	0.001
ESR	Mean ± S.D	17.1 ± 4.9	14.2 ± 4.3	20.0 ± 3.5	0.001
Random Blood Sugar	Mean ± S.D	120.7 ± 17.8	123.5 ± 21.9	117.8 ± 11.9	0.105
AST	Mean ± S.D	22.4 ± 8.8	19.5 ± 6.7	25.3 ± 9.7	0.001
ALT	Mean ± S.D	19.9 ± 4.9	20.6 ± 5.2	19.3 ± 4.5	0.166

Group A1 = Sertaline, Group A2= Fluoxetine

Table No.2: Laboratory findings at Wk-0 and Wks-24 in both groups

Parameters	SSRIs (n=100)							
	Group A1 (n=50)				Group A2 (n=50)			
	Wk - 0		Wks - 24		Wk - 0		Wks - 24	
	No	Mean ± S.D	No.	Mean ± S.D	No.	Mean ± S.D	No.	Mean ± S.D
BMI	50	27.2 ± 2.78	46	27.4 ± 2.91	50	26.3 ± 2.73	47	26.4 ± 2.64
Hemoglobin	50	11.9 ± 1.61	46	12.3 ± 1.52	50	10.9 ± 1.27	47	11.4 ± 1.09
ESR	50	14.2 ± 4.34	46	18.3 ± 4.88	50	20.0 ± 3.53	47	21.8 ± 4.45
RBS	50	124 ± 21.8	46	122 ± 6.7	50	118 ± 11.9	47	122 ± 6.7
AST	50	19.5 ± 6.7	46	25.8 ± 5.6	50	25.3 ± 9.7	47	25.9 ± 5.6
ALT	50	20.6 ± 5.2	46	35.5 ± 10.1	50	19.3 ± 4.5	47	40.9 ± 11.3

Group A1 = Sertraline, Group A2= Fluoxetine

Only AST and ALT were statistically significant from Wk-0 to Wk-24 $p<0.05$ in group A1 while only ALT was significantly changed ($p<0.05$) from Wk-0 to Wk-24 in group A2.

Table No.3: Level of depression according to HRSD, SRQ and BSI with SSRIs in both groups

Level of depression		SSRIs (n=100)			P-Value
		Overall all (n=100)	Group A1 (n=50)	Group A2 (n=50)	Group A1 vs. A2
HRSD	Mild to Moderate (13-17)	7	6 (12%)	1 (2%)	0.050
	Severe (>17)	93	44 (88%)	49 (98%)	
	Mean ± S.D	24.0 ± 4.6	22.2 ± 4.1	25.8 ± 4.4	0.001
SRQ	Normal (M<=4 or F <=8)	27	15 (30%)	12 (24%)	0.499
	Abnormal (M>.4 or F>8)	73	35 (70%)	38 (76%)	
	Mean ± S.D	9.4 ± 1.8	9.2 ±1.7	9.7 ± 1.9	0.213
BSI	Mean ± S.D	21.7 ± 2.6	21.4 ± 2.3	22.1 ± 2.7	0.150

Table No.4: Level of depression according to HRSD from Wk - 0 to Wks -24 in Group A1 and A2), values in Mean, S.D

HRSD	SSRIs					
	Group A1			Group A2		
	No.	Mean	S.D	No.	Mean	S.D
0	50	22.2	4.1	50	25.8	4.4
2	50	21.6	4.2	50	24.9	4.3
4	50	18.9	3.6	50	22.7	4.4
6	49	16.4	3.9	50	21.1	4.3
8	49	15.2	3.9	50	18.7	3.8
10	48	14.3	4.0	49	17.3	3.9
12	48	13.5	3.7	49	16.0	3.7
14	47	12.9	3.5	49	15.5	3.7
16	47	12.5	3.4	48	15.1	3.4
18	47	12.0	3.2	48	14.8	3.5
20	47	11.6	3.2	47	14.6	3.6
22	46	11.0	3.0	47	14.4	3.8
24	46	10.7	3.0	47	14.1	4.1

Group A1 = Sertraline, Group A2= Fluoxetine. HDRS (Hamilton Rating Scale for depression)

Sertraline vs. Fluoxetine

Improvement in depression during the 24 wk study, measured by Hamilton depression scale and Self Reporting Health Questionnaire did not differ significantly between the two groups. Gradual improvement was seen from 2nd week onwards with highly significant improvement in both scores at the end of treatment in both drug groups.

Compliance in both groups was more than 90% and no difference was noted between the 2 groups.

When adverse effects were compared it was seen that in psychic adverse effect, decreased duration of sleep was most commonly seen with Fluoxetine group while in Sertraline group sleepiness and increased duration of sleep were most common. In neurological adverse effects tremors were most often seen with Sertraline group while with Fluoxetine paresthesias were most commonly observed. In autonomic nervous system, nausea was the most commonly observed adverse effects seen maximally with both drug groups. Weight loss was seen more with Sertraline group while headache was seen with both groups (Table No.6).

Table No.5: Comparison of Hamilton Rating Scale for Depression (HDRS) and Self Reporting Questionnaire (SRQ) in both groups at Wk 0 to Wks-24 in SSRIs

Parameters		Overall all (n=100) Mean ± S.D	Group A1 (n=50) Mean ± S.D	Group A2 (n=50) Mean ± S.D
HRSD	Wks – 0	24.0 ± 4.6	22.2 ± 4.1	25.8 ± 4.4
	Wks – 24	12.4 ± 3.9	10.6 ± 3.0	14.1 ± 4.1
	P-Value	0.001	0.001	0.001
SRQ	Wks – 0	9.4 ± 1.8	9.2 ± 1.8	9.7 ± 1.9
	Wks – 24	7.2 ± 1.6	6.7 ± 1.2	7.6 ± 1.8
	P-Value	0.001	0.001	0.001

Group A1 = Sertraline, Group A2= Fluoxetine

Table No.6 : Most Common Treatment Emergent Adverse Effects: Incidence in Clinical Trial between group A1 and A2

	A1 (Sertraline)						**A2 (Fluoxetine)**					
Body system/Adverse event	**(n = 50)**						**(n = 50)**					
	Wk 4	**Wk 8**	**Wk 12**	**Wk 16**	**Wk 20**	**Wk 24**	**Wk 4**	**Wk 8**	**Wk 12**	**Wk 16**	**Wk 20**	**Wk 24**
Psychic Disorders												
↓ed duration of sleep	5	5	5	5	4	4	7	6	7	4	4	4
Asthenia	5	5	3	4	4	4	2	2	2	2	2	2
↑ed duration of sleep	6	5	2	3	3	3	3	3	3	2	2	2
Sleepiness	4	6	4	5	4	5	3	3	3	1	1	1
Tension	2	2	3	2	1	1	2	1	1	1	1	1
Neurologic Disorders												
Dystonia	2	2	1	0	0	0	1	1	1	1	1	1
Paresthesias	5	5	2	1	1	1	7	7	6	6	6	6
Tremors	4	4	4	1	1	1	1	0	0	0	0	0
Autonomic Nervous System Disorders												
↑ed salivation	2	2	3	3	3	3	2	1	1	1	1	1
Nausea	10	9	2	0	0	0	8	11	4	3	2	2
Orthostatic dizziness	2	2	5	3	3	3	2	2	3	3	3	3
↑ed sweating	2	4	4	6	5	5	3	2	3	6	6	6
Constipation	0	2	2	2	2	3	4	7	1	1	1	1
↓ed salivation	0	0	0	1	1	1	3	3	6	5	5	5
Palpitations	1	1	1	2	3	3	0	4	1	2	3	3
Other Disorders												
Weight loss	0	1	2	4	6	5	0	0	1	1	2	3
Headache	3	0	0	1	1	0	4	3	1	1	0	0
Weight gain	0	0	0	1	1	2	0	0	1	1	1	1

DISCUSSION

The use of antidepressant medications and the resulting costs have increased dramatically in recent years, partly because of the introduction of selective serotonin reuptake inhibitors (SSRIs).

This is the first reported independent study comparing selective serotonin receptor blockers like Sertraline and Fluoxetine in Pakistani population suffering from major depression.

This study shows that females suffer from depression much more than males and the average age lies between 40 yrs and 45 years that is coinciding with the study of Naqvi in 2007 (20).

The clinical response with both drugs was excellent with minimal adverse effects.

Although HDRS scores were highly significantly reduced from week 0 – week 24 in both groups with p value <0.001 but it was seen that improvement with group A1 occurred earlier than group A2. In both groups there is a gradual improvement throughout the 24 week study period.

With SRQ scores it was noted that both groups were again highly efficacious at the end of the study period with p value <0.001.

4 patients in group A1 did not complete the study period because of adverse effects or for the reason that there was no improvement in their symptoms. 3 patients in group A2 did not complete the study for the same reasons. Nausea was the most common adverse effect leading to discontinuation of treatment.

Patient compliance was not a significant problem in any of the groups.

When efficacy of Sertraline was compared with Fluoxetine, it was seen that Sertraline was numerically better than Fluoxetine but this was not statistically significant. Both drugs caused a highly significant improvement in HDRS scores with remission in the disease.

Both Sertraline and Fluoxetine are highly and almost equally efficacious as seen by the HDRS and SRQ scales.

This study is in accordance with the study of Fava and Rosenbaum et. al. (21). who compared these drugs and found that patients demonstrated similar baseline to endpoint improvement in HAMD-17 scores. Each treatment was similarly effective in improving depression. Overall, both treatments were well tolerated.

Our study is in accordance with the combined analysis published in 2003 showing treatment response similar with sertraline and fluoxetine, although sertraline may be slightly more advantageous in severe depression (22).

In another study comparing efficacy and safety of Sertraline and Fluoxetine conducted in 1993, (23) the results were very similar to our study. Although there was a numerical advantage for Sertraline on several efficacy measures, there was no statistically significant difference found between the treatment groups. The incidence of adverse events was similar for both treatments; 40.4% for Sertraline and 39.3% for Fluoxetine. However, adverse events were generally rated by patients as of lower severity in the Sertraline group. In addition, for the Fluoxetine group, there was a higher incidence of agitation, anxiety and insomnia than for Sertraline. Sertraline was considered to be better tolerated than Fluoxetine overall, since only 9.6% of Sertraline-treated patients discontinued treatment due to therapy failure whereas in the Fluoxetine-treated group this figure was 19.6%. By contrast, 13.5% of Sertraline-treated patients discontinued prematurely because of clinical improvement, compared with 10.7% of Fluoxetine-treated patients.

In contrast to our study, Geddes and Cipriani (24) show that SSRIs do not work much better than placebo. This may be because they have considered short term randomized trials of SSRIs in children and adolescents while we conducted our study only in adults.

In our study both Sertraline and Fluoxetine treated patients demonstrated robust antidepressant responses as reflected by large decreases in ratings on the HDRS and SRQ. None of the patients in both groups demonstrated any suicidal thoughts. Both drugs were well tolerated. The levels of AST and ALT were raised at the end of the study from the baseline, and trials of these drugs for longer duration should be done to know its significance. Although, further studies with larger groups of patients and comparisons with placebo are required to establish the superiority of one drug over the other but we suggest that Sertraline which showed earlier improvement in scores and is cost effective as well may be a better choice to treat major depression.

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Original Article

The Effectiveness of Elastic Rubber Band Ligation Technique in Cases of Internal Haemorrhoids

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ABSTRACT

Objective: To study the effectiveness of the elastic rubber band ligation technique in cases of internal haemorrhoids.
Study Design: A prospective study.
Place and duration of study: This study was conducted at Jinnah postgraduate medical center Karachi during 2007-2008.
Materials and Methods: A total of 70 patients of varying degrees haemorrhoids of either sex were taken randomly. In 20 out of the 70 cases open Haemorrhoidectomy was performed by low ligation and excision (after due preparation of the patients) and in 50 cases elastic rubber band technique was performed. Tablet Bisacodyl 4-6 tablets stat were given to the patients at night before the procedure. No anesthesia was used. This procedure was performed in Left lateral position or in knee-elbow/jack-knife position.
Results: Patients with elastic rubber band ligation method were discharged at the same day (average stay was only for the procedure), with minimum complains, and post operative complications were found negligible (Pain 28, haemorrhage 6%, discomfort 14%). In contrast average stay in the cases of Haemorrhoidectomy was 5 – 26 days and complications ranged between pain and haemorrhage (95%), discharge (15%), retention of urine (10%) and faecal incontinence (15%). No case of faecal incontinence and retention of urine was observed in cases of elastic rubber band ligation technique.
Conclusion: Elastic rubber band ligation as an Out Patient procedure, is effective, economical easily performable, with minimum complications and is without hazards of anaesthesia.
Key Words: Piles, Elastic rubber band ligation, Haemorrhoidectomy

INTRODUCTION

'Haemorrhoids' is one of the most frequently occurring disease and affects one in every twenty five persons (Cohen-Zig, 1985) and 50% of population above 50 years of age (Goliger, 1948).
Hippocrates applied term "Haemorrhoids" to the flow of blood from veins of anus. Actually the word 'Haemorrhoid' is a Greek word derived from 'Haem' means bleeding and 'rhoid' means flowing. Piles is an other name given to the disease (Latin word meaning ball) which also seems to have been used widely by the public at the time of John Ardere (born 1307 A.D.). He was first to have used this term in his writings (Edwards et al 1983).
In our society Haemorrhoids are called 'Bawaseer' and are classified in two types

i. Khooni Bawaseer (Bleeding Haemorrhoids).
ii. Badi Bawaseer (Prolapsed haemorrhoids)

Various, methods of treatment are available e.g. Injection Sclero- therapy, Suppositories cream, Infra-red coagulation, Cryo-surgery, Elastic band ligation and Haemorrhoidectomy.
Since 1888 apart from surgery conservative treatment are universally used (Dennison 1989). Conservative treatment of Internal Haemorrhoids by ointment, Injective sclerotherapy or Rubber band ligation is effective in 89% of patient while in External Haemorroids conservative treatment is effective in 66% (Ahmed et al 1990) of the cases.
Most usual treatment is haemorrhoidectomy, but majority of population is illiterate and afraid of anesthesia and operation and the wound may also take one and half month to heal and in some cases postoperative dilation is needed.
As far as the convenience of patient is considered one of the easier procedure in the treatment of Haemorrhoids is elastic rubber band ligation. No hospitalization is needed, minimum complication, time consumption, require less investigations and patient may be discharged on the same day.
Every person wants easy and quick economical, procedure, which should not interfere with their work. Elastic rubber band ligation has minimal side effects, good results, easy, less time consuming and economical. So keeping all these facts in mind we conducted this study to look for cost effectiveness of rubber band ligation with other procedures.

MATERIALS AND METHODS

This (prospective study) was conduced at surgical unit one at the Jinnah postgraduate medical center Karachi. A Performa specially designed was used, including name, age, sex, occupation, socioeconomic status, address, presenting complains, history of presenting complaints, family history, physical examination, systemic examination, laboratory investigation, and treatment. Investigations were performed when found necessary i.e. Blood Complete Picture, Erythrocyte Sedimentation Report, Urine Detail Report, X-ray Chest, Electrocardiogram, Stool Detail Report, and Ultrasound of abdomen, Sigmoidoscopy and Barium enema.

Total seventy cases were selected (selection criteria). Twenty cases were operated for (Haemorrhoidectomy) and on fifty cases elastic rubber band ligation was performed. No special preparation was necessary for elastic rubber band ligation, except Tablet Bisacodyl 4-6 tablets at night before the procedure. No anesthesia was used. This procedure was performed in left lateral position or in knee-elbow/jack-knife position.

After per rectal examination liquid paraffin lubricated proctoscope was introduced and haemorrhoids were grasped and banded. Not more than two haemorrhoids were banded at a time in order to reduce the pain edema and circumferential large ulceration. At least three weeks gap was observed between banding procedure. Ligated haemorrhoids sloughed off mostly on the seventh day after procedure.

Twenty patients selected for Haemorrhoidectomy were admitted and prepared for operation. Open Haemorrhoidectomy of low ligation and excisation type was done.

Statistical analysis was done on computer soft ware SPSS.

RESULTS

From this study we observed following important facts.

Age and sex incidence of the Haemorrhoids:

From our study it became apparent that Haemorrhoids are most prevalent between 3rd and 4th decades of life i.e. 31% and 28% of the cases respectively and 82% of case were male and 18% female. (Table.1)

Signs and symptoms:

Following signs and symptoms were found in our patients, bleeding and prolapse (95%), pain (35%), discharge (15%), itching (6 %) of the cases. Anaemia was present in over all (40 %) of our cases.

Degree of piles:

1st and 2nd degree were found in 28% of cases and 3rd degree piles were found in 44% of cases.

Professional back ground:

We found that 40% of cases were field workers. Other professions affected are as follows, office worker 24%, shopkeepers 16%, house wives 6%, farmer 2% and teachers 2 %. (Table.2)

History of Past illness:

History of Past illness of patient showed hypertension 11%, chest problems 5%, asthma 3%, and diabetes 2% of cases.

Regarding hospital stay:

In cases of rubber band ligation most of patients were treated as out patients and hospital stay was not required. One case was admitted for three days for Sigmoidoscopy and colonoscopy and blood transfusion and was discharged after rubber band ligation and two cases were admitted for transfusion before the rubber band ligation because their hemoglobin was low and were discharged after rubber band ligation.

Post operative complains in the cases of rubber band ligation: Following complaints were found, pain 28%, discomfort 14%, haemorrhage 6% itching and discharge in 2% of the cases respectively as shown in table 3.

Post operative complains in the cases of Haemorrhoidectomy:

Haemorrhage and pain in 95% of cases, itching and discharge in 15% of cases, acute retention of urine in 10% cases and faecal incontinence in 15% of cases.

Number of days off from work:

In cases of rubber band ligation 68% reported to work on next day and only 10% remained off work for two weeks time after procedure. In cases of Haemorrhoidectomy off the work figure was 4, 5, 6, and 8 week i.e. 25%, 15%, 5%, 20% respectively.

DISCUSSION

Haemorrhoids are one of the most common diseases of mankind. Actual incidence is unknown since many patients with minor symptoms do not come for advice, many even with severe discomfort do not show their anal region due to shyness (Hawley, 1973).

Haemorrhoids have been more commonly observed in people of lower socioeconomical group and in people with profession which involves working for long period of time in standing position (Table 2).

Peak incidence is in 3rd and 4th decade and predominant in male (as mentioned in Table 1) this is supported by Teramoto et al 1989.

It is observed from the study that disease neither has rising incidence with age as was observed by Hass et al 1984 and nor is prevalent in all age group as observed by Melvin 1985. Youngest patient was 17 years old and oldest was 85 years old.

Rubber band ligation was introduced by Blaisdell in 1958 and refined by Barron in 1963. This procedure

was observed as good procedure in patients suffering from ischaemic heart disease, hypertension, chronic bronchitis, asthma, jaundice, diabetes mellitus etc.

In our experience most patients with rubber band ligation needed only an initial outpatient visit at which assessment and treatment was under taken followed by single visit two weeks later. The cost effectiveness, safety and ease of treatment for both patients and doctors combined with good clinical results which have been obtained have increased the popularity of rubber band ligation. Rubber band ligation also provides a lasting effect of rectal bleeding, haemorrhoidal prolapse anal pain pruritis and soiling. This technique can be performed in the out patients in a few minutes without anaesthesia. One great advantage of ligation therapy of internal haemorrhoids is that so many patients can get relief from their haemorrhoids despite serous illness or advanced age. This procedure is as effective as haemorrhoidectomy and rather more effective than sclerotherapy, cryosurgery (Sims et al 1981, Williams and Crapp 1975). This is in agreement with our findings.

Hospital stay is negligible while after Haemorrhoidectomy minimum hospital stay was 5 days and maximum stay was 26 days.

Main criticism of rubber band ligation is that it does nothing to remove skin covered component of pile or an associated skin tag. However lower remaining portion of haemorrhoid may under go some shrinkage the bothering part may latter be removed under local anaesthesia as an out door procedure.

Slipping of bands is a disadvantage of this procedure. The incidence of slippage can be reduced to some extent by better selection criteria. As 2nd and 3rd degree Haemorrhoids are more suitable for this procedure. Cases of 1st degree haemorrhoids are not suitable because sufficient tissue is not available for application of bands

For third degree haemorrhoids with large skin component rubber band has very limited value so there is no substitute for surgical treatment. Fourth degree hemorrhoid is not suitable for rubber band ligation.

CONCLUSION

From our study it become apparent that elastic rubber band ligation is very important technique as far as the haemorrhoids are concerned. It is Out Patient procedure with excellent results. It has easy procedure which can be performed even in patients suffering from other systemic illnesses (as mentioned earlier in the results and dicussion). As anaesthesia is not given so anaesthesia hazards are no more there. Its postoperative complications were found minimal and is very much economical procedure.

Table No.1: Age Incidence of Patients

Age Range Between = 17-85 Years			
Total Number of Cases 70			
Serial Number	Age range	Number of patient	Percentage
1.	11-20	04	05%
2.	21-30	09	12%
3.	31-40	22	31%
4.	41-50	19	28%
5.	51-60	10	14%
6.	61-70	04	05%
7.	71-80	01	02%
8.	81-90		02%

Table No.2: Occupational History of Patients

Total Number of Cases= 70			
Serial number	Occupation	Number of cases	Percentage
1.	Field workers	26	38%
2.	Office Worker	16	22%
3.	Shopkeepers	12	17%
4.	House wives	07	10%
5.	Farmers	05	07%
6.	Teachers	03	05%
7.	Contractor	01	01%

Table No.3: Postoperative Coplications after Rubber Band Ligation

TOTAL NUMBER OF CASES=50			
Serial number	Complications	Cases	Percentage
1.	Haemorrhage	3	6%
2.	Pain	14	28%
3.	Discomfort	7	14%
4.	Itching	1	2%
5.	Discharge	1	2%
6.	Acute retention	0	0%
7.	Faecal incontinence	0	0%

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Corrigendum

Subject: Amendment in Designation of second author Dr. Dure Shahwar

The article titled "The effect of Co2 Pneumoperitoneum on End Tidal Co2 (ETCO2), Arterial Blood Pressure and Heart Rate During Laparoscopic Cholecystectomy Under General Anaesthesia" published in the month of March 2011, Vol.22 No.3 on pages 17-22. The designation of Dr. Dure Shahwar on Serial No.2 may please be read as Assistant Professor of Anaesthesia instead of Assoc. Prof. of Surgery.