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EDITORIAL:

THE QUITE REVOLUTION IN SURGICAL NUTRITION

Advances in molecular medicine genomics and system biology has led to a doubling of high quality information every 3 years. This has led interalia, to a quiet revolution in our approach to nutrition; in particular surgical nutrition.

Food is the most powerful unregulated thing in the world and is used more extensively than any other proven medication for better; but too often for worse. What is not realized is the magnitude of its effect which is not immediate. The high quality Boyd-Orr study started in 1937 has clearly demonstrated halving of incidence of all forms of cancer by fruit and low caloric intake. This effect would have been even greater but for the British propensity for "boiling the hell out of their vegetables". Weight loss similarly decreases deaths by degenerative diseases and cancer by 25% over as short a period as 10 years.

The role of surgeon in initiating life style changes is particularly important in Pakistan with its double disease load; even more relevant in south Asia is that bariatic surgery will cure up to 93% of all type II diabetes – obesity linked type 2 diabetes can no longer be regarded as a chronic progressive medical condition. Of more immediate concern to the individual surgeon is the question of preoperative starvation, postoperative alimentation and nutrition in the seriously ill patient with SIRS, CARS and MODS. It is becoming increasingly clear that the gut is the motos of MODS.

Eighty percent of patients admitted to surgical wards are starved in hospitals particularly the very ill – which sounds more like medical deprivation rather than modern medical management. Furthermore much of this starvation is medically instituted for fear of acid inhalation during anesthesia and postoperative ileus.

A Major change has taken place in the recent years. This change has been led by anesthetists who allow liberal food intakes upto hours before surgery. Similarly a major move is towards early alimentation postoperatively as this has a protective effect against MODS and its consequences; particularly infection. Total parenteral nutrition has proved to be a management of last resort with many problems and complications. The renewed interest in postoperative alimentation has seen the rise of such additives as glutamine and arginine – mainly with positive results in this difficult field of study.

As gut deprivation appears to be a potent factor in the development of MODS. There are now many advocates of prophylactic jejunostomy or jejunal intubation rather than reviewing this procedure as a last resort. Enthusiasts even advocate early enteral feeding in the presence of distal large bowel fistulas.

The take home message for surgeons is that a major body of work suggests that our traditional approach to pre and postoperative care is illogical in sick patients, many will be deleterious and that better results are obtained with early feeding. In addition, the modern surgeon has to initiate prophylaxis of later problems by lifestyle nutritional alterations- particularly obesity. Also bariatic surgery cures most type 2 diabetics.

PETER BALLIE

AN EXPERIENCE OF LONG TERM CENTRAL VENOUS LINES IN CHILDREN

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ABSTRACT:
Long term central venous (LTCVL) lines are silicone catheters placed for various indications in children who need repeated vascular access for a long time. In two years period 20 Hickman lines were placed in children. The indications included chemotherapy, parenteral nutrition, immunotherapy and haemodialysis for chronic renal failure. One line was removed after 6 weeks with a primary sepsis. One line got broken by the improper handling. One line was removed after 6 months with a true line sepsis. Most of the long central lines were successful in achieving the goal of their placement and were removed after the completion of therapy.

KEY WORDS: Venous access, Central line, Intravenous access devises

INTRODUCTION

Long term central venous lines are essential component of management of children for parenteral nutrition, chemotherapy, immunotherapy, haemodialysis etc. There is lot of fear in use of these lines in our setup. These have become popular in private sector and many hospitals are now using them routinely for long term venous access. Local studies have proved its safety and efficacy in our setup. This study was therefore conducted to further emphasize the fact that use of these lines is safe and affective way of achieving long term venous access in children.

PATIENTS AND METHODS

Hickman or Broviac lines were placed in 18 children. Strict aseptic measures were ensured during the placement of these lines. Any form of bleeding diathesis was corrected preoperatively by platelets or fresh frozen plasma transfusions. Patients with thrombocytopenia also received platelet transfusions during surgery. The procedure was performed under general anaesthesia by standard technique. Single or double lumen Hickman catheter was used. The catheter was primed with heparinized saline and tunnelled through a separate stab incision. The catheter tip was cut short to be placed at the distal level of superior vena cava just above the right atrium. The catheter position was confirmed by the image intensifier at the distal end of the superior vena cava. Standard three dose antibiotic prophylaxis was ensured in all the children. Line was available for use after the surgery and patients were allowed home on next day in most cases.

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RESULTS

In 18 children 20 Hickman catheters were placed during two years period. Among these 18 were single lumen and two had double lumen catheter. There were 11 male and 7 female patients. The age ranged from 2 months to 13 years with a mean age of 6 years. The indication for line insertion included venous access for chemotherapy, immunotherapy or bone marrow transplantation for aplastic anaemia, necrotizing enterocolitis for total parenteral nutrition, haemodialysis for chronic renal failure. There was no line failure on technical grounds. The average duration of line insertion was 45 minutes. Of all the lines inserted, 6 children grew bacteria from the entry site of the line 6 weeks to 6 months after insertion. These included Staph. aureus in two patients, Streptococcal pyogenese in one patient, E coli in one patient, Pseudomonas one patient and Listeria in one patient. Out of these true line sepsis was noted in two patients one with aplastic anaemia and other of chronic renal failure. The first child started having high grade fever 4 weeks after line insertion. Blood and line cultures grew Staph. aureus. This was treated aggressively with

broad spectrum antibiotics through the line with little improvement. Therefore the line was removed. The child with renal failure developed generalized sepsis and showed deterioration even after adequate antibiotic treatment via the line and the catheter was then removed which also grew Staph. aureus. Child improved after removal of catheter. All the other children who had colonization at the entry site were symptom free. This gave a true sepsis rate of 6%. One line developed a leak by improper handling after 3 months and had to be removed. All the other lines were successful in achieving their purpose of insertion and were either removed after the completion of therapy or the babies were taken to other hospitals for treatment of their pathology. Lines were reinserted in both the patients who developed complications. Both of them later remained well.

DISCUSSION

Long term central venous lines are silicone catheters used in patients who need venous access for long periods. Broviac and Hickman catheters are available in Pakistan. These can be used for months and years for IV nutrition therapy, chemotherapy, immunotherapy, blood sampling and haemodialysis[1,2]. The use of these lines in babies and children for parenteral nutrition has changed the whole scenario of their management[3,4]. In babies long peripheral central lines provide other route of intravenous therapy[5,6]. In children long term central lines are helpful in achieving good patients' compliance by avoidance of multiple pricks and fears related to it. It also enables out patients chemotherapy and home parenteral nutrition as no pricks are involved[6]. Furthermore the double lumen lines can be used for blood sampling and for giving different types of intravenous fluids simultaneously. The prerequisite in the placement of LCVL are ensuring sterilization and aseptic techniques during the procedure to avoid line related sepsis[7,8,9] which is the most serious complication related to the insertion of LCVL. Beside this there are other complications associated with line placement[10,11,12]. These include haemorrhage[13], pleural effusion[14], chylothorax [10], cardiac temponade[15,16], osteomyelitis[17], air embolism[18], knotted guide wires[19] to mention a few. The incidence of these complication however is low and related mostly to percutaneous insertion of LCVL in babies and small children [20]. Open insertion of line under direct vision poses much less a problem. The overall incidence of serious complications varies from 4 to 15 percent[11,12]. The most serious and dreadful complication is line related sepsis.[21] It not only requires removal of an expensive line but also poses a real threat to the life of the patients who are often immuno-compromised and debilitated[22]. Studies have however shown that even in the severely immuno-compromized patients the incidence of line sepsis can be relatively low if care is taken in insertion and maintenance of line[21]. In most developed countries the incidence of primary line sepsis ranges from 5 to 15 %[10,11]. On average insertion of a LTCVL will cause 20 to 25 thousand rupees in a private setup. Line sepsis will not only waste that money but may also threaten the life of patient by uncontrolled sepsis if the infected line is not removed. In over study less than 7% primary sepsis rates, is comparable with other international studies[11,12].

Initially it was thought that in all the patients who had line sepsis the catheter has to be removed. It is no longer true. With the use of new broader spectrum antibiotics through the line it is now possible to control line sepsis and removal may not be necessary in all the children with line sepsis [23].

Another complication of LCVL is occlusion of line tip. This is one of the major problems with the line. Often the line may act as a one way catheter where the fluids can be infused through the line but blood can not be drawn. This is usually due to a small clot at the catheter tip causing ball valve effect. This is an avoidable complication. The line should be flushed with about 10 ml of saline after use and then with 5 ml of heparinized solution and then lock the line. Even a partially blocked line may be opened by flushing streptokinase or urokinase through the line[24,25].

Cost of LCVL is a serious consideration in our patients. But the line itself can help in decreasing the cost of treatment by offering day care chemotherapy and haemodialysis. It also avoids the cost of repeated admissions. Long term central venous access also ensures a pain free route for venous sampling and therapeutic procedures.

Port-a-caths are other devices for long term venous access [26]. They have subcutaneous ports and thus give the freedom for sports and normal activity. They need special needles and topical local anaesthetic creams which are often not available in local markets. Beside this they are more expensive. They are however better devises for long term venous access with less incidence of line related complications and will probably replace the external Broviac and Hickmann catheters in older children.

In summary long term central lines provide excellent vascular access for selected children. Its does have its limitations and may only be used for definite indications.

REFERENCES

1. Rao S, Alladi A, Das K, Cruz AJ: Medium and long term central venous access in children. Indian Pediatr 2003; 40: 41-4.

2. Tawil KA, Gillam GL. Gastroschisis: 13 years' experience at RCH Melbourne. J Paediatr Child Health 1995; 31: 553-6.

3. Vanderhoof JA, Matya SM. Enteral and parenteral nutrition in patients with short-bowel syndrome. Eur J Pediatr Surg 1999 ;9:214-9

4. Chowdhary SK, Parashar K, Buick RG, Gornall P, Corkery JJ: Central-venous access through the peripheral route in surgical neonates: an audit of 125 consecutive lines from a regional neonatal centre. Pediatr Surg Int 2001 17:433-5.

5. Chow LM, Friedman JN, Macarthur C, et al. Peripherally inserted central catheter (PICC) fracture and embolization in the pediatric population. Canada. J Pediatr 2003;142:141-4

6. Alhimyary A, Fernandez C, Picard M, Tierno K, et al. Safety and efficacy of total parenteral nutrition delivered via a peripherally inserted central venous catheter. Nutr Clin Pract 1996 11:199-203

7. Fallat ME, Gallinaro RN, Stover BH, Wilkerson S, Goldsmith LJ. Central venous catheter bloodstream infections in the neonatal intensive care unit. J Pediatr Surg 1998 ;33:1383-7

8. Shaul DB, Scheer B, Rokhsar S, Jones VA, et al. Risk factors for early infection of central venous catheters in pediatric patients. J Am Coll Surg 1998 ;186:654-8

9. Kocent H, Corke C, Alajeel A, Graves S: Washing of gloved hands in antiseptic solution prior to central venous line insertion reduces contamination. 2002 ;30:338-40

10. Island ER, Church JA, Shaul DB: Short-term complications of central line placement in children with the human immunodeficiency virus. J Pediatr Surg 2001.;36:1777-80

11. Burney IA, Khurshaidi N, Akbar MT, Bhatti FN, Siddiqui T, Sophie Z: Complications of in-dwelling venous access devices: a single institution experience. J Pak Med Assoc 2001 ;51:434-7

12. Tobiansky R, Lui K, Dalton DM, Shaw P, Martin H, Isaacs D. Complications of central venous access devices in children with and without cancer. J Paediatr Child Health 1997 ;33:509-14

13. Margolis JO, Bloch EC. Haemothorax following central line placement. Paediatr Anaesth 1997;7:178

14. Paw HG: Bilateral pleural effusions: unexpected complication after left internal jugular venous catheterization for total parenteral nutrition. Br J Anaesth 2002;89:647-50

15. Kabra NS, Kluckow MR: Survival after an acute pericardial tamponade as a result of percutaneously inserted central venous catheter in a preterm neonate. Indian J Pediatr 2001 68:677-80

16. Cupitt JM. An unusual complication of a central venous catheter in a neonate. Paediatr Anaesth 2000;10:665-8

17. Upadhyay V, Chandran H. Is central venous access in childhood osteomyelitis associated with increased morbidity? Pediatr Surg Int 1998 14:202-3

18. Laskey AL, Dyer C, Tobias JD: Venous air embolism during home infusion therapy. Pediatrics 2002 ;109 :E15

19. Hoogsteden L, Filshie J, Querci della Rovere G. Knotted guidewire--A complication of Hickman line insertion. Anaesthesia 1996 ;51:713

20. Wiener ES, McGuire P, Stolar CJ, et. al. The CCSG prospective study of venous access devices: an analysis of insertions and causes for removal Pediatr surg.1992; 27:155-163

21. Decker MD, Edwards KM: Central venous catheter infections. Pediatr Clin North Am 1988 35:579-612,

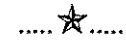
22. Island ER, Church JA, Shaul DB. Short-term complications of central line placement in children with the human immunodeficiency virus. J Pediatr Surg 2001 36:1777-80

23. Berrington A, Gould FK: Use of antibiotic locks to treat colonized central venous catheters. J Antimicrob Chemother 2001 48:597-603

24. Haire WD, Lieberman RP, Lund GB, et al. Obstructed central venous catheters restoring function with 12 - hour infusion of low dose Urokinase. Cancer 1990; 66:2279

25. Larwood KA, Anstey CM, Dunn SV.Managing central venous catheters: a prospective randomised trial of two methods. Aust Crit Care 2000 13:44-50

26. Bermas H, Albrecht RM, Vogt D. An evaluation of two methods for chronic central venous access device placement. Am J Surg 1999 ;178:560-3



A PLACEBO-CONTROLLED CLINICAL TRIAL ON NIMESULIDE IN OSTEOARTHRITIS

NIGHAT KAFIL, KAUSAR AAMIR, SHAH MURAD, JAMAL ARA*, SAADIA ANJUM**

ABSTRACT:
Osteoarthritis is a chronic, progressive articular disorder characterized by pain. The prevalence of this most common joint disease rises with increasing age and occurs in approximately 85% of people between 75- to 79-year of age. Simple analgesics are useful in patients with mild disease, although nonsteroidal anti-inflammatory drugs (NSAID) are the main stay of therapy. Nimesulide is an NSAID that has demonstrated clinically significant anti-inflammatory, analgesic and antipyretic activity in a variety of painful inflammatory conditions, including osteoarthritis. We compared nimesulide with placebo in groups of 30 patients each and were able to see a highly significant improvement in the parameters of pain at rest, pain on movement and tenderness while placebo group showed non-significant improvement in all the symptoms in a study conducted for 90 days. Nimesulide was well tolerated with mild side-effects.

KEY WORDS: Cyclooxygenase, Prostaglandins, Visual analog scale

INTRODUCTION

Osteoarthritis (OA) is a spectrum of clinical entities, ranging from focal chondral defects to established arthrosis resulting from hyaline cartilage failure[1]. OA is by far the most common form of arthritis and represents a major cause of morbidity and disability in the elderly[2,3,4,5]. It represents failure of the diarthrodial (movable, synovial lined) joint[6] OA is designated primary (idiopathic) when no cause is obvious and is the most common form of the disease, and secondary when it follows a demonstrable abnormality attributable to an underlying cause although indistinguishable from idiopathic OA[6,7]. Joints most frequently involved are those of the spine, hips, knees and hands. The disease is confined to one or only a few joints in the majority of patients. Common patterns of joint involvement include the nodal and non-nodal types of primary generalized OA with prominent involvement of the knees and hands as well as OA confined to the knees or hips[8]. Though some people with OA have an obvious inflammatory component, most have little or no inflammation. Despite this and the known association of non-steroidal anti-inflammatory drugs with gastrointestinal complications of hemorrhage, perforation and occasionally death, NSAIDs are widely prescribed[9].

Nimesulide is an NSAID that selectively inhibits cyclooxygenase2. The inducible form of the enzyme found almost exclusively in inflammatory tissues but largely devoid of physiological activity in healthy tissues in which cyclooxygenase 1 plays important regulating role (particularly gastric and renal physiological control). Most NSAIDs block both cyclooxygenase 1 and cyclooxygenase 2, and as a result they impair the production of prostaglandins critical to gastric mucosal protection and renal function, which results in clinically significant adverse reactions especially the risk of gastrotoxicity. Nimesulide is the leading molecule of a new chemical class, the sulphonanilides, which has shown a significant inhibitory selectivity towards cyclooxygenase 2 without affecting cyclooxygenase 1. This results in equivalent efficacy against pain and inflammation but with a better safety profile particularly at the gastrointestinal level[10].

The main objective of this study was to evaluate patient responses to nimesulide in terms of overall efficacy, pain relief, immediate side effects and general well being.

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MATERIALS AND METHODS

Tablet nimesulide (Nise) 100mg were obtained from PharmEvo (Pvt) Ltd. Pakistan, and placebo capsules packed by K. Ahmed and Sons, Karachi were used in the study. The study was conducted in the Department of Pharmacology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical College, Karachi. A total of 60 patients of either sex, between 35 – 80 years suffering from OA of at least one knee joint were selected. The study period was for 90 days. Patients were divided into 2 groups, Group A and Group B of 30 patients each. Group A received tablet nimesulide 100mg twice daily while Group B received the placebo treatment once a day for 90 days. Each patient gave written consent to join the study and was given a 72-hour wash out period for any medication that the patient might have been taking previously. Only patients suffering from primary OA of at least one knee joint were selected while secondary cases were excluded with the help of various tests like ESR > 40, rheumatoid factor, serum uric acid, blood glucose etc. On entering the study, x – rays of the affected knee joint of each patient in antero-posterior and lateral weight bearing position were obtained. Laboratory tests like Hb%, ESR, blood urea and bleeding time were performed on day 0, 45 and finally on day 90. Patients were asked to come for follow-up visits every fortnightly while statistical analysis of data was performed between day 0, 30, 60 and day 90. Parameters of pain at rest, pain on movement and tenderness were evaluated by 4-point scale which is:

0 = None: no pain felt by the patient
1 = Mild: Slight pain which can be tolerated
2 = Moderate: Pain causing discomfort to the patient
3 = Severe: Unbearable pain

The 4-point scale for pain was converted for measurement on Visual analog scale (VAS)[11].

0 = Up to 0.5 cms
1 = 0.6 – 3.5 cms
2 = 3.6 – 6.6 cms
3 = 6.7 – 10 cms

Of the various methods for measuring pain VAS seems to be the most sensitive [11,12,13,14,15,16]. For tenderness, local examination of knee was performed and pain felt at specific sites such as patella in full extension of foot and knee and on medial condyle of femur. 4-point scale for tenderness indicates –

0 = Very slight
1 = Definite
2 = Wincing
3 = Withdrawal

This was converted on VAS as in measurement of pain.

RESULTS

Results obtained in the present study are summarized in Table I -III. Within the group statistical analysis was performed by "Paired t test" while inter group analysis was done with "Student t test". The Mean ± SEM values are shown on day 0 and then on day 30, 60 and day 90 with percentage change between day 0 and day 90 while p values were taken out between day 0 – day 30, day 0 – day 60, and day 0 – day 90.

Nimesulide produced highly significant ($p<0.001$) improvement in pain at rest, pain on movement and tenderness only after 30 days of treatment which was sustained until the end of therapy. There was a 79%, 60% and 70% reduction in pain at rest, pain on movement and tenderness respectively (Table I).

One patient was lost to follow up. Four patients (13.80%) complained of mild side-effects which did not result in any break in therapy. Of these 4 patients, 2 complained of diarrhea, 1 of edema of both legs and 1 of heartburn that was relieved when milk was taken with the medicine.

TABLE-I THERAPEUTIC EFFICACY IN ALL PARAMETERS AT DAY 0, 30, 60 AND DAY 90 WITH TABLET NIMESULIDE 100 mg b.i.d. (GROUP A)

PARAMETERS	DAY 0	DAY 30	DAY 60	DAY 90	% Change Day0-Day90	p value		
						Day0-30	Day0-60	Day0-90
Pain at rest (cm)	1.93 ±0.17	1.67 ±0.17	1.02 ±0.13	0.40 ±0.13	— 79.27	<0.001 HS	<0.001 HS	<0.001 HS
Pain on movement (cm)	6.76 ±0.27	5.59 ±0.29	3.59 ±0.29	2.67 ±0.34	— 60.50	<0.001 HS	<0.001 HS	<0.001 HS
Tenderness	5.17 ±0.43	3.64 ±0.34	2.47 ±0.32	1.53 ±0.37	— 70.40	<0.001 HS	<0.001 HS	<0.001 HS

All the values are expressed in mean ± S.E.M. units.
HS – Highly significant, b.i.d. – twice daily, cm - centimeter
Negative (-) sign indicates reduction of symptoms compared between day 0 – day 90.

TABLE-II THERAPEUTIC EFFICACY IN ALL PARAMETERS AT DAY 0, 30, 60 AND DAY 90 WITH PLACEBO (GROUP B)

PARAMETERS	DAY 0	DAY 30	DAY 60	DAY 90	% Change Day0-Day90	p value Day0-30	p value Day0-60	p value Day0-90
Pain at rest (cm)	1.89 ±0.20	2.02 ±0.25	1.89 ±0.20	1.93 ±0.21	2.11	>0.05 NS	>0.05 N.S	>0.05 NS
Pain on movement (cm)	5.83 ±0.32	5.39 ±0.27	5.39 ±0.28	5.81 ±0.31	— 0.34	<0.05 S	<0.05 S	<0.05 S
Tenderness	4.56 ±0.37	3.98 ±0.37	4.20 ±0.33	4.57 ±0.35	0.21	<0.05 S	<0.05 NS	<0.05 NS

All the values are expressed in mean ± S.E.M. units.
S – Significant, NS – Non significant, cm. – centimeter.
Negative (-) sign indicates reduction of symptoms compared between day 0 – day 90.

Treatment with placebo did not produce any significant ($p>0.05$) improvement in any of the parameters at the end of therapy although pain on movement showed significant ($p<0.05$) improvement between day 0 – day 30 and day 0 – day 60, and tenderness also showed significant ($p<0.05$) improvement after 30 days of treatment but between day 0 – day 90 they became non-significant. There was a 2% improvement in tenderness while a worsening of 2% in pain at rest, and 3% in pain on movement at the end of therapy vide Table II. Three patients were lost to follow-up. 5 patients (18.51%) complained of side-effects, 2 of itching over the whole body, 1 of headache and 1 of body ache in general.

When Group A and Group B were compared with each other between day 0 – day 90, in all the parameters highly significant ($p<0.001$) improvement with Group A was seen, (Table III).

TABLE-III COMPARISON OF PERCENTAGE CHANGE AND P VALUE BETWEEN GROUP A, AND GROUP B, IN ALL THE PARAMETERS BETWEEN DAY 0 AND DAY 90

GROUPS	DAY - 0	DAY - 90	% Change Day0-Day90	p Value Day0-Day90
PAIN AT REST				
Group A (n=29)	1.93±0.17	0.40±0.13	-79.27	<0.001 H.S
Group B (n=27)	1.89±0.20	1.93±0.21	2.11	>0.05 N.S
PAIN ON MOVEMENT				
Group A (n=29)	6.76±0.27	2.67±0.34	-60.50	<0.001 H.S
Group B (n=27)	5.83±0.32	5.81±0.31	-0.34	>0.05 N.S
TENDERNESS				
Group A (n=29)	5.71±0.43	1.53±0.37	-70.40	<0.001 H.S
Group B (n=27)	4.56±0.37	4.57±0.35	0.21	>0.05 N.S

Group A – Tablet Nimesulide, Group B – Placebo, n - number of patients, cm. – centimeters, H.S – Highly significant, N.S – Non-significant.

DISCUSSION

In this study, the therapeutic effects of nimesulide were quickly realized after 30 days of treatment which were sustained until the end of the study period. Indeed, nimesulide rapidly reduced pain at rest (79%), and tenderness (70%) but a relatively lesser effect on pain on movement (60%) was observed. Placebo produced non-significant improvement in all the parameters.

The improvements in efficacy variables demonstrated with nimesulide in this study are in close agreement with other clinical investigations in OA. For example, Blardi et al.,[17] in 1992 compared nimesulide with placebo in 40 OA patients in a treatment cycle of 90 days. Reduction in all the parameters was highly significant ($p<0.001$) at the end of the study period. Our study is also in accordance with the studies of Quattrini and Paladin[18] Bennett and Villa[19] and Kriegel et al[20] where nimesulide was associated with a statistically significant ($p<0.05$) improvement in the signs and symptoms of pain and tenderness. The benefits achieved were essentially similar to those in our study. Non-significant ($p>0.05$) improvement with placebo was seen.

The significant and highly significant improvement in symptoms as early as 30 days after commencement of therapy may be due to inhibition of the release of oxidants from activated neutrophils and has a scavenging effect on hypochlorous acid without affecting neutrophils function. Nimesulide also decreases histamine release from tissue mast cells and inhibits the production of platelet-activating factor by human basophils. It inhibits the release of stromelysin and blocks metalloproteinase activity.[21] In addition to their anti-inflammatory and analgesic benefits, it may have a protective effect in OA through the inhibition of apoptosis in chondrocytes.[22]

Our study is not similar to the study of Dreiser and riebenfeld [23] where nimesulide gave non-significant results in all the parameters as their study was for only 2 weeks. In the current investigation, nimesulide was well tolerated. Four patients treated with it complained of side-effects while 5 patients treated with placebo complained of side-effects. No pathological changes in hematology and blood chemistry tests were found. A judgment of good/fair of 86% was recorded by us for nimesulide group and only 16% for placebo group. It is suggested that additional comparative studies are required to confirm Nimesulide's long term efficacy and safety profile.

REFERENCES

1. Cole BJ, Harner CD. Degenerative arthritis of the knee in active patients: evaluation and management. J Am Acad Orthop Surg; 1999 7:389-402.
2. Jaffe HL. Degenerative Joint Disease. In: Metabolic, Degenerative, and Inflammatory Diseases of Bones and Joints. Henry LJ, Ed. (1st edition), Lea and Febiger, Philadelphia; Ch. 25, 735-745.
3. Preidler KW, Resnick D. Imaging of Osteoarthritis. Radiologic Clinics of North America;1996 24:259-271.
4. Da Camara CC, Dowless GV. Glucosamine sulfate for osteoarthritis. Ann Pharmacother; 1998 32:580-587.
5. Hochberg MC, McAlindon T, Dieppe PA, et al . Osteoarthritis: New Insights. Ann Intern Med; 2000 133:726-735.
6. Brandt KD (2001). Osteoarthritis. In: Harrison's Principles of Internal Medicine. Braunwald E, Hauser SL, Fauci AS, Longo DL, Kasper DL, Jameson JL, eds. (15th edition), McGraw-Hill, New York; Ch. 321, 1990. 1987.
7. Solomon L (2001). Osteoarthritis and related disorders. In: Apley's System of Orthopaedics and Fractures. Solomon L, Warwick D, Nayagam S, Eds. (8th edition), Arnold, London ;Ch. 5, .2001127-134.
8. Nuki G, Ralston SH, Luqmani R (2001). Diseases of Connective Tissues, Joints and Bones. In: Davidson's Principles and Practice of Medicine. Haslett C, Chilvers ER, Hunter JAA, Boon NA. Eds. (18th edition), Churchill Livingstone, UK; Ch. 12, 1999, 826-829.
9. March L, Irwig L, Schwarz J, Simpson J, Chock C, Brooks P .n of 1 trials comparing a non-steroidal anti-inflammatory drug with paracetamol in osteoarthritis. BMJ; 309: 1994 1041-1045.
10. Rabasseda X. Safety profile of nimesulide: Ten years of clinical experience. Drugs of Today; 1997 33:41-50.
11. Huskisson EC . Measurement of Pain. Lancet 1974 II; 1127-1131.
12. Hewer AJH, Keele CA, Keele KD, Nathan PW. A Clinical method of Assessing Analgesics. Lancet;1949 431-435.
13. Vaz AL. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthrosis of the knee in out-patients. Curr Med Res Opin; 1982 8:145-149.
14. Wigler I, Neumann L, Yaron M. Validation study of a Hebrew version of WOMAC in patients with osteoarthritis of the knee. Clin Rheumatol; 1999 18:402-405.
15. Bellamy N, Cambell J. Syrotuik J. Comparative study of self-rating pain scales in osteoarthritis patients. Curr Med Res Opin; 1999 15:113-119.
16. Pincus T, Koch GG, Sokka T et al. A randomized, double-blind, crossover clinical trial of diclofenac plus misoprostol versus acetaminophen in patients with osteoarthritis of the hip or knee. Arthritis Rheum; 2001 44:1587-1598.
17. Biardi P, Gatti F, Auteri A, Di Perri T .Effectiveness and tolerability of nimesulide in the treatment of osteoarthritic elderly patients. Int J Tissue React; 1992 14:263-268.
18. Quattrini M, Paladin S. A double-blind study comparing Nimesulide with Naproxen in the treatment of osteoarthritis of the Hip. Clin Drug Invest; 199510:139-146.
19. Bennett A, Villa G. Nimesulide: an NSAID that preferentially inhibits COX-2, and has various unique pharmacological activities. Expert Opin Pharmacother; 2000 1:277-286.
20. Kriegel W, Korff KJ, Ehrlich JC, et al. Double-blind study comparing the long-term efficacy of the COX-2 inhibitor nimesulide and naproxen in patients with osteoarthritis. Int J Clin Pract; 2001 55:510-514.
21. Bevilacqua M, Magni E. Recent contributions to knowledge of the mechanism of action of nimesulide. Drugs; 1993 46:40-47.
22. Mukherjee P, Rachita C, Aisen PS, Pasinetti GM. Non-steroidal anti-inflammatory drugs protect against chondrocyte apoptotic death. Clin Exp Rheumatol; 2001 19:7-11.
23. Dreiser RL, Riebenfeld D. Nimesulide in the treatment of osteoarthritis. Double-blind studies in comparison with piroxicam, ketoprofen and placebo. Drugs; 1993 46:191-195.

THE CLINICAL SIGNIFICANCE OF PRE-OPERATIVE SERUM CA-125 IN OVARIAN CANCER

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ABSTRACT:
The objective was to study the value of serum CA125 levels in the initial workup of women with ovarian cancers. Over a two year period (1st January 1999- 31st December 2000), preoperative serum CA125 level was analysed in 23 women with clinical suspicion and those with an adnexal mass diagnosed as ovarian malignancy postoperatively on histopathology at Lady Dufferin Hospital,Karachi.
Among patients with an age range 13-72 years (mean: 44 years.) 82 % had epithelial ovarian cancer. CA125 was raised in 80 % of stage 1, 78% of stage 111 and 100% stage1V diseases. We therefore recommend preoperative serum CA 125 estimate in all cases of suspicious adnexal masses.

KEY WORDS: CA125, Ovarian cancer

INTRODUCTION

Ovarian cancer is the fifth leading cause of all cancer deaths in women and the commonest female genital tract malignancy in our study. Two thirds of the women have advanced disease at the time of diagnosis[1]. CA125 is an antigenic determinant high molecular weight glycoprotein recognized by a monoclonal antibody (OC125). CA125 is elevated in 82% of women with advanced (stage111or1V) ovarian cancer[2] and it is also elevated, although less frequently in women with earlier disease[3]. Pre-operative CA125 levels are recommended for providing a baseline in subsequent followup.

This study was designed to evaluate preoperative CA125 levels, as an additional diagnostic tool in diagnosing ovarian malignancy.

PATIENTS AND METHODS

This study comprised 33 women aged 13-72 years (mean 44Year) diagnosed as having ovarian malignancy over a two year period. Preoperatively these women had routine blood and urine analysis, whole abdomen and pelvis ultrasound, chest x-ray, renal and liver function tests in addition to serum CA125 assays.

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Their preoperative levels of serum CA125 were reviewed after surgery, histopathology and adequate staging.

RESULTS

During a two year period (January 1999-December 2000) 81 women presented with malignancies of the female genital tract. (Table 1) Ovarian cancer was the commonest (40%) malignancy. Primary ovarian tumor was found in 80% of these women. Secondary and recurrent ovarian tumor constituting 10% each.

Twenty three women with primary ovarian cancer were reviewed in whom record was available. Epithelial carcinoma was present in 84% of the cases followed by sex-cord (12%) and germ cell tumor (4%). 50% of the patients presented in stage1 (Table II). A raised serum CA125 was seen in 80% of epithelial, 33% of sex-cord and 100% of germ cell tumors. 78% of women in stage III and 100% in stage IV disease presented with raised serum CA 125 levels. The highest level (5542 U/ml) was observed in a 38 year old presenting as stage III

TABLE-I FEMALE GENITAL TRACT MALIGNANCY		
CANCERS	NUMBER	%
Ovary	31	39
Cervix	18	22
Endometrium	26	32
Others	6	7
TOTAL	81	-

moderately differentiated endometroid cystadeno-carcinoma. There was no correlation of CA 125 levels with age or any particular cell type.

TABLE-II	STAGE OF PRIMARY OVARIAN TUMOR	
STAGE	NUMBER	%
1	13	50
11	-	-
111	10	38
1V	3	12

DISCUSSION

Ovarian cancer is the leading cause of gynecologic cancer mortality in the world. At the time of diagnosis the disease has usually spread beyond the ovary and is associated with a five year survival of 33% compared to 90% for stage 1 tumors. Even after the advent of newer therapies there has been little change in its survival rates. 90-95% of ovarian malignancies are epithelial in origin, these include serous mucinous endometroid, clear cell mixed epithelial and undifferentiated histologies. 10 - 15% of these are termed borderline or of low malignant potential because of their limited metastatic tendency and a higher 5 year survival rate.

The various tools used in the diagnosis of an ovarian malignancy include clinical examination, abdominal and transvaginal ultrasonography with trans vaginal color doppler and serum CA 125 measurement. 'Studies have shown that when CA 125 levels were evaluated in healthy patients, patients with benign pelvic masses and those with malignant masses a 93.3% sensitivity and 79.7% specificity were achieved using the usual threshold of greater than 35 u/ml. In studies of mass, known or suspected ovarian cancer, the reported sensitivity of CA125 in detecting stage 1 and II cancers are 29-75% and 67-100% respectively.[5,6] In our review we found that the introduction of transvaginal ultrasonography (TVU) has helped to detect pelvic masses earlier as apparently 50% of ovarian malignancs were still in stage I. Serum CA 125 is an important additional diagnostic tool, perhaps hastening laparotomy to reach a final diagnosis. Studies of stored serum have found that about half of the women who developed ovarian cancer had raised serum CA 125 levels 18months -3years before the diagnosis[3,7]. However ,evidence regarding CA 125 levels in asymptomatic women is still lacking. It must be kept in mind that CA 125 is also raised in other conditions as benign masses (e.g. uterine fibroids , endometrioisis, pancreatic pseudocyst, pulmonary hamartoma) and in non gynecologic cancers (e.g. pancreas, stomach, colon, breast). But women with adnexal masses with or without symptoms and particularly those falling in the high risk group have high serum CA 125 levels, need to be counseled preoperatively about the risk. Surgery should be performed in tertiary care centers where facilities for trained histopathologist, oncologist and adequate followup are available.

Until other tests with better sensitivity and specificity are available reliance on serum CA 125 will continue. It is needed as a combination with TVS and doppler study in high risk women for the purpose of screening . Even if it fails to prevent the disease it can be aimed to detect stage I disease where the survival rate is 95-100%.

CONCLUSION

Pre-operative serum CA 125 is an important additional diagnostic tool. Even though its role in diagnosis and screening has not been defined, it is of value when used in combination with ultrasound in both circumstances. Serial studies and a higher cut off value may be considered preoperatively as an indication for laparoscopy or laparotomy.

REFERENCES

1. Pettersson F, ed. Annual report on the results of treatment of gynecologic cancer. Int J Gynecol Obstet 1991; 36:238-277.
2. Bast RC, Klug TL, St John E, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian carcinoma. N Engl J Med 1983;309:883-887.
3 Zurawski VR Jr Orjester H, Andersen A,et al.Elevated serum CA125 levels prior to diagnosis of ovarian cancer neoplasia: relevance for early detection of ovarian cancer. Int J Cancer 1988;42:677-680.
4 Chen DX, Schwartzz PE, Li XG, et al; Evaluating CA 125 levels in differentiating malignant from benign tumors in patients with pelvic masses.Obstet Gynecol 1988;72:23-27
5. Zurawski VR Jr, Knapp RC, Einhorn N,et al, An initial analysis of preoperative serum CA 125 levels in patients with early stage ovarian carcinoma.. Gynecol Oncol 1988;30:7-14.
6. Schilthuis MS, Aalders JG, Bouma J, et al. Serum CA125 levels in epithelial ovarian cancar:relation with findings at second-look operations and their role in the detection of tumor recurrence.Br J Obstet Gynaecol 1987;94:196-201.
7. Helzlsouer KJ, Bush TL, Alberg AJ, Bass KM, Zacer H, Comstock GW. Prospective study of serum CA 125 levels as tumor markers of ovarian cancer.JAMA 1993;306:1030-1034.

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A STUDY TO ASSESS THE EFFECT OF DIET RESTRICTION ON LIPID LEVEL IN OBESE SUBJECTS

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ABSTRACT:

Both over weight and obesity should be regarded as a potential health hazard. Purpose of this study was use to evaluate weight reduction and blood lipid profile after one and three months of diet regimen in slimming clinics. Fifty obese subjects of both genders (age between 35 to 50 years) were randomly selected from the British Slimming Clinic in Lahore. Their lipid profile including total lipid, cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were analysed twice by standard kit method (Merck and Bohringer). Blood samples were taken, first at the time of joining the clinic and then after three months. It was observed that lipids level (total lipids,cholesterol, triglyceride, HDL and LDL-chol) except the level of the HDL-chol was decreased in male subjects. Whereas in female obese subjects the lipids level except the level of LDL-chol were significantly decreased. It is therefore concluded that changes in diet from high saturated fat diet, high caloric, high cholesterol and high carbohydrate diet would be advantageous for an individual as it lessens the weight and decrease the risk of obesity related disease.

KEY WORDS: Lipid profile, Obesity

INTRODUCTION

Obesity has been defined for adults as a weight of 120% or more of the acceptable range for sex and height. Overweight and obesity are commonest nutritional disorders in both developing and developed countries accounting for 5-39% of adults at different ages, though prevalence of figures vary[1]. Both overweight and obesity should be regarded as a potential health hazard. These can be associated with raised fasting blood sugar levels and increased blood pressure[2]. Although coronary heart disease (CHD) is multifactorial, there is an increasing risk of morbidity from CHD with over weight. Changes in body weight affect two of the risk factors; blood pressure and serum cholesterol, both of which are reduced with weight loss[3]. There is overwhelming and accumulating evidence for a genetic component in overweight, especially in cases of moderate to severe obesity[4].

Individual energy requirement varies widely from the mean recommended allowances for any age or weight, and depends in part on energy expenditure and growth. Physical inactivity may contribute to the development of obesity in the community and a decline in activity levels will mean that those who are susceptible to weight gain will be at risk[1]. Besides, social, psychological, endocrinological, and metabolic factors all contribute to the prevalence of over weight in the community as a whole, and several factors may be involved in any individual who is overweight[5].

The accumulation of fat has serious drawbacks from the view point of health, morbidity, aesthetics, enjoyment of life and social acceptance. As a result, weight control has become a matter of interest, not only among medical and public health workers, but also among the public. The slimming center of Lahore and different cities of Pakistan boast an ability to reduce weight from 15-20 lbs. within a month. The treatment at these centers consists of diet in powder or capsule form along with a restricted diet schedule.

Purpose of study was to evaluate weight reduction and blood lipid profile after one and three months of diet regimen in slimming clinics.

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MATERIALS AND METHODS

Fifty obese subjects of both genders (age between 35 to 50 years) were randomly selected from the British Slimming Clinic in Lahore. Their lipid profile including total lipid, cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were analysed twice by standard kit method (Merck and Bohringer). Blood samples were taken, first at the time of joining the clinic and then after three months.

The data has been statistically analysed using student 't' test[6].

RESULTS

Table 1 shows mean weight and blood pressure in both obese male/female subject and control subjects. Mean body weight of both male/female was vary high (226.91 Vs 149.40 and 199.40 Vs 121.80) as compared to normal control and it showed a highly significant difference (P<0.001). Blood Pressure of male was the same (approx. 126/81.00 mmHg) when compared with their controls. In female obese blood pressure was raised (125.80/81.0 Vs 118.50/76.26) as compared to control subjects but it showed no significant difference.

TABLE-I VALUES OF BODY WEIGHT AND BLOOD PRESSURE (B.P)

Variables	Male obese (25)	Male control (20)	Female obese (25)	Female control (20)
Weight (lbs) (mean)	226.19±11.01*	149.40±7.58	199.40±7.58*	121.80±2.30
Blood pressure (mmHg)	126.00/81.25 ±1.08/1.08	125.75/80.25 ±1.16/0.85	125.80/81.00 ±4.53/1.00	118.50/76.26 ±1.50/1.39

*P<0.001= Highly significant difference

Table II shows the changes of biochemical parameters like total cholesterol, HDL-Cholesterol (HDL-C), LDL-Cholesterol (LDL-C), triglyceride and total lipid in male patient from 1-3 months. It was observed that level of total cholesterol is non significantly decreased (229.12 VS 217.52) after 3 months as compare to level in I month. Level of LDL-C decreased (179.08 Vs 163.86) with a highly significant difference (P<0.001). It was noted that level of HDL-C was non significantly increased with the level of triglyceride and total lipid also non significantly decreased in 1-3 months regimen.

TABLE-II CHANGES IN LIPID PROFILE OF MALE SUBJECTS FROM 1-3 MONTHS VALUES EXPRESSED AS MEAN-S.E.M.

Parameters	1 Month	3 Months
Total Cholesterol (mg%)	229.12±3.85	217.52±3.96
HDL Cholesterol (mg%)	32.00±0.72	36.29±0.71
LDL Cholesterol (mg%)	179.08±3.49	163.86±3.62*
Triglyceride (mg%)	125.08±4.97	122.88±5.03
Total Lipid (mg%)	698.16±9.96	687.88±9.88

*P<0.001= Highly significant difference

Table III shows changes of biochemical parameters in female patients from 1-3 months. It was observed that the level of total cholesterol is non significantly decreased at 3 months as compared to the level of 1 month. Level of LDL-C also decreased as compared to the level of 1 months with a highly significant difference (P<0.001). It was found that level of HDL-C was increased and this shows highly significant difference (P<0.001). Level of triglyceride and total lipid also decreased in 1-3 months regimen with a highly significant difference (P<0.001).

TABLE-III CHANGES IN BIOCHEMICAL PARAMETERS OF FEMALE SUBJECTS FROM 1-3 MONTHS VALUES EXPRESSED AS MEAN-S.E.M.

Parameters	1 Month	3 Months
Total Cholesterol (mg%)	235.56±4.56	225.28±4.94
HDL Cholesterol (mg%)	36.14±0.82	40.26±0.78*
LDL Cholesterol (mg%)	179.94±4.54	166.68±5.04*
Triglyceride (mg%)	101.24±1.75	93.22±1.50*
Total Lipid (mg%)	672.20±5.21	641.64±5.83*

**P<0.001= Highly significant difference

DISCUSSION

It is generally agreed that there is a direct relationship between obesity and risk factors like sex, blood pressure and lipid profile. It has been observed that most male/female subjects were obese and between the age of 32-34 years. The findings are in accord with the reported work where it was observed that obesity develops with increasing age and is characterized by increased food intake and declining energy expenditure via activity and metabolism[7]. A significant decrease of weight in both male and female subject was observed after 3 month as compared to their weight at 1 month.. These findings are in agreement with the study of a group of workers[8,9].

The diet introduced in a weight reducing program contained low fat and carbohydrate and high protein with vitamin and mineral supplement. After 2 weeks moderate exercise was also added. Duration of exercise was increased with the passage of time. Our study observed changes in lipid profile in male subjects at 1 and then after 3 months. It was also seen that level of total cholesterol and LDL-C were significantly decreased in both sexes. These finding are in accord with a number of studies where a single set of dietary modification achieves satisfactory lipid reduction in hypertriglceridemic and hypercholesterolimic subjects[10,11]. Our findings are in contrast with the reports of earlier workers which showed that weight reduction promptly decreases cholesterol synthesis and leads to a transitory reduction of serum cholesterol but does not have a permanent effect[12,13]. Exercise was also taken as a parameter. It was observed that regular exercise also has its effect on weight and biochemical factors. It was has it also demonstrated[14] that

exercise alone could achieve weight loss in a group of women who were taking regular exercise for 30min to 1hour.

Changes in lipoprotein (HDL, LDL-C) were also observed in both male and female subjects after 3 months when compared to month 1. Level of HDL-C showed significant increase after the same period. These findings are in agreement with a number of studies indicating that level of HDL is favorably influenced by weight loss as a result of diet and exercise in both sexes[9,14]. Another report indicated that in both sexes the ratio of serum LDL to serum HDL cholesterol were substantially and favorably influenced by weight loss prompted by diet plus exercise[9]. In women, level of HDL-C was significantly increased while level of LDL-C cholesterol is significantly decreased after 3 months. Study is in confirmatory with conclusions of a group of workers[15] who reported that plasma lipoprotein metabolism, in women, is influenced by the circulating concentration of gonadal steroids. Changes in serum estrogens and androgen concentration, resulting, either from alteration in gonadal status or from administration of estrogens gonadal steroid, have been shown to be associated with changes in serum lipoprotein level. Our findings contrast with study[10] that observed no change in level of HDL cholesterol in women undergoing diet and exercise.

CONCLUSION

Changes in diet from high saturated fat diet, high caloric, high cholesterol and high carbohydrate diet would be advantageous for an individual as it lessens the weight and the high rate of coronary vascular disease and other obesity related diseases.

REFERENCES

1. Kaushik VK. Readings in Food, Nutrition and Dietetics. Vol 1, Book Enclave India, pp77-79
2. Cohen N, Flemenbaum W. Obesity and hypertension: Demonstration of a floor effect. Am J Med 1986, 80:177.
3. Davidson MJ. Principal and Practice of Medicine. Edinburgh Churchill Living Stone Co London. 1999, 802
4. Guyton AC. Text book of Medical Physiology. 8th ed. W B Saunders Co Philadelphia. 1999, 667
5. Isselbacher KJ, Adams RD, Braunwald E et al. Harrison's Principles of Internal Medicine. McGraw Hill International Book Co. London. 2000, 411-416
6. Steel RGD Torrie JH. Principles and procedures of statistics. McGraw Hills Book Co. Inc New York. 1984, 85
7. Godsland IA, Wynn V, Crook D. Sex, Plasma lipoprotein and atherosclerosis prevailing assumption and out standing questions. Am Heart J: 114:1467-1503
8. Murchison S. Hyperlipdaemia. Br Med J 1985;290:537-38
9. Wood PD, Stefanick ML and Williams PT. The effect of plasma lipoprotein of a prudent weight reducing diet in over weight men and women. N Eng J Med 1991 325:461-466
10. Tai ES, Fok AC, Chu R and Tan CE. A study to assess the effect of dietary supplementation with soluble fibre on lipid level in normal subject with hypercholesterolemia. Ann Acad Med Singapore. 1999, 28:209-13
11. Akanji AO, Al-Shayji IA and Knman P. Metabolic disorders Int J Obes Relat Metab Disord. 1999,23:855-62
12. Streja DA, Boyko E, Rabkin SW. Changes in plasma high density lipoprotein cholesterol concentration after weight reduction in grossly obese subjects Br Med J.1980, 281:772-3
13. Liuzzi G, Savia G, Tajliaferi M, Lucantoni R, Berselli ME, Petroni ML Medici CD. Obesity and lipid metabolism Int J Obes Relat Metab Disord. 1999, 23:1066-73
14. Bender AE Brooks LJ. Body weight control: The physiology of clinical treatment and prevention of obesity. Churchill Livingstone, Edinburgh. 1987, 53-60
15. Stanfield PS and Hui YH. Nutrition and dietary therapy. Self Instructional Modules. 2nd ed Jones Barlet Publishers Boston 1992, 38-48

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ROLE OF TLC AND C-REACTIVE PROTEIN IN THE DIAGNOSIS OF ACUTE APPENDICITIS

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ABSTRACT:

Acute appendicitis is one of the most common intrabdominal affections seen in surgical departments, which can be treated easily if accurate diagnosis is made in time otherwise delay in diagnosis and treatment can lead to diffuse peritonitis. A study was done to determine the role and predictive value of total leucocyte count (TLC) and C-reactive protein (CRP) in the diagnosis of acute appendicitis. All patients admitted with a clinical diagnosis of acute appendicitis and underwent appendectomy between September 2000 to March 2001 were included in this study.

All patients presented within 24-36 hours of onset of pain. Out of 150 patients studied, 99 (66%) were males and 51 (34%) females. Age distribution was between 3years to 69years with a mean age of 20.3 years. In all patients who proved to have acute appendicitis (positive) TLC were found to be significantly high (p=0.025). The serum CRP levels were found to be either normal or at the high values of reference range (p=<0.001). In the group, with per-operative findings of gangrenous or perforated appendix both TLC count and CRP levels were found to be significantly high. These were compared with the group for negative appendecectomies i.e. 19 patients. 17 out of these 19, (89.4%) had normal TLC and CRP levels. The sensitivity and specificity of serum CRP were 98% and 87.5% respectively with a predictive value (PV) of positive test almost 98%

KEY WORDS: C-Reactive Protein, TLC, Appendicitis

INTRODUCTION

Usually the diagnosis of acute appendicitis is made on the basis of history, physical examination along with few supportive investigations like the total leucocyte count. It has been well-documented that there are certain acute phase-reaction proteins which are raised in various inflammatory conditions. These proteins include C-reactive protein. If C-reactive protein can be added to the already existing laboratory tests then the diagnosis of acute appendicitis with clinically suggestive signs can be made with fair degree of accuracy and as such unnecessary appendectomies can be avoided. Studies consistently show that 80-85% of adults with appendicitis have a WBC count greater than 10,000 while neutronphilia greater than 75% occurs in up to 78% of patients[1]. In adult patients who have had symptoms for more than 24 hours, a normal CRP has a negative predictive value of approximately 97-100%[2]

The purpose of this study was to study the pre-operative leucocyte count and C-reactive protein in patients suspected of having acute appendicitis and to evaluate the preoperative diagnosis assurance and the predictive value of these tests in patients with acute appendicitis who undergo appendectomy later on.

Both TLC and CRP are easily available blood tests, not very expensive and the definite advantage that they can be obtained within about 1-2 hours and thus the surgeon on call can decide about the management of patients suspected of acute appendicitis.

PATIENTS AND METHODS

A study was conducted on patients with a clinical diagnosis of acute appendicitis, who underwent appendectomy later on. This data was collected between the September 2000 and March 2001. A total of 150

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patients were operated for acute appendicitis at the Department of Surgery, Rawalpindi General Hospital. Incidental and interval appendicectomies were excluded from the study.

Provisional diagnosis of acute appendicitis was made on the basis of history, physical findings and relevant clinical data. During operations, the degree of inflammation of the appendix was noted, along with relevant operative findings. Appendix was sent for histopathological examination. For statistical purposes these 150 patients were assigned into 3 groups (a) Patients with normal appendix. (b) Patients with uncomplicated acute appendicitis (C) Patients with complicated acute appendicitis i.e. gangrenous/perforated appendix. The number of patients with normal TLC and CRP values, raised total leucocyte count, raised CRP level and raised both TLC and CRP values raised were calculated in each of these groups. All patients received perioperative antibiotics. For complicated cases IV antibiotics were continued for 5 days.

Blood samples for the quantitative serum CRP measurements were collected before operation. The decision to operate was made independent of the CRP levels as these results were not given to the operating team. The laboratory staff were not aware of the clinical findings, decisions and outcome. The histological diagnosis of acute appendicitis required the involvement of the muscularis layer of appendix in inflammation. In all cases at least two sections one from proximal and other from distal end were studied.

RESULTS

In the sample of blood taken just preoperatively leucocyte count was determined by an electronic cell counter device (Coulter Counter T, 790; Coulter Electronics Hialeah, Florida, USA). The upper limit of reference values for TLC was $9x10^9$/L for females and $10x10^9$/L for males.

Quantitative serum CRP was measured by the Nephelometer (Array Protein Chemistry System, Backman Instruments, Fullerton CA, USA). Normal CRP level in our laboratory is 0-0.8 mg/dl. Levels above 2.0 mg/dl were considered as high.

The final results were analysed using one-way ANOVA for multiple comparisons. The differences between the three groups were determined by paired student 't-test' and 'Statview – 4.02' statistical package was used for analyses. 'P-value' of <0.05 were considered to be statistically significant.

Out of 150 patients studied, 99 (66%) cases were males and 51 (34%) females. Age range was 3years to 69years with a mean age of 20.3 years. In the male patients, the commonest age group was 11years – 22years (50.5%). As regards the females, age ranged between 6 years to 68 years, with a mean age of 20.8 years. Commonest age group was from 11 years to 20 years (50.9%).

130 (86.6%) cases had histopathologoical evidence of inflammation of the appendix, whereas in 18 (12%) cases appendix was found to be normal or these were the cases of negative exploration. In 2 (1.3%) cases peroperative findings differed from the findings of acute appendicitis. One patient a 32 years male had terminal ileitis and the other case had nodular appearance of the appendix which proved to be a case of carcinoid tumour on histopathology.

In all patients who proved to have acute appendicitis (positive) TLC were found to be significantly high (p=0.025). The serum CRP levels were found to be either normal or about the high values of reference range (p=<0.001). In the group, with per-operative findings of gangrenous or perforated appendix both TLC count and CRP levels were found to be significantly high. These were compared with the group for negative appendectomies: 17 had normal TLC and CRP levels. Only 2 patients showed high CRP levels one with a ruptured ovarian cyst and the other with terminal ileitis. The mean CRP levels in patients with positive explorations was (6.47 ± 3.43 mg/d) and 1.8 ±1.32 mg/dl in patients with normal appendix or negative explorations. (Table I)

TABLE-I HISTOPATHOLOGY OF APPENDIX

	Negative	Positive	p-value
WBC ($x10^9$/dl)*	10.0±3.04	13.68±6.07	0.025
CRP (mg/dl)*	1.8±1.32	6.47±3.43	<0.0001

** Values expressed as Mean±SD*

DISCUSSION

C-reactive protein was first found in the serum of patients suffering from pneumonia caused by streptococcus pneumoniae[3]. Together with other acute phase-proteins, the serum level of CRP rises in response to any tissue injury. It also increases in response to infections (bacterial and viral) and also in non-infectious conditions like myocardial infarction, malignancies and rheumatic disorders[4]. CRP level increases within 8 hours of the onset of tissue injury, peaks in 24-48 hours and remains high as long as there is continuing infection or tissue destruction[5]. Incidence of normal appendix increased to about 14% when 2 cases suspected to have acute appendicitis had carcinoid and terminal ileitis. Lower incidence of normal appendix in our study may be contributed to careful clinical assessment, by performing abdominal ultrasound in about 40% of female patients

with doubtful diagnosis pre-operatively. Ultrasound facility was not available round the clock; therefore, ultrasound could not be performed in all females and young children to rule out other causes of pain lower abdomen.

In our study, in all patients who had histologically proven acute appendicitis, both preoperative leucocyte count and serum CRP were significantly high. However 16 patients (10.6%) had been operated on for a clinical suspicion of acute appendicitis, even though the preoperative leucocyte count and CRP values were normal. Interestingly, almost all these patients had negative explorations peroperatively and later on histopathological examination the appendix were found to be uninflammed. At the same time, in all patients with acute appendicitis either leucocyte count or CRP value, or both, were above normal limits. Thus, although there was a clinical suspicion of acute appendicitis, normal leucocyte count and CRP value excluded acute appendicitis with a predictive value of almost 100 percent in the present study. Thus it can be inferred that a normal preoperative CRP level is not associated with acute appendicitis[7]. Appendectomy is not recommended for patients with a normal leucocyte count and CRP value, even if acute appendicitis is suspected clinically. These patients should be treated by careful clinical observation, and additional leucocyte count and CRP measurements. If clinical symptoms or signs of acute appendicitis continue and the leucocyte count and/or CRP value increase above the upper limit of the reference interval, the patient should undergo laparoscopy. Otherwise continued observation can be recommended with confidence. These findings are in accord with a recent retrospective study which showed no rise in pre-operative WBC count or CRP levels in all patients in whom the removed appendix was normal.

In a similar study, done on a cohort of 227 patients serial measurements of TLC and CRP levels was done every four hours in patients with suspected acute appendicitis. It was reported that it was unusual to find a normal CRP level after 08 hrs of observation in the presence of acute appendicitis[8]. Moreover, in a double-blind prospective trial Albu et al in 1994 studied 56 patients, the result of CRP levels were not made available to the surgeon during the patient's hospital stay. They concluded that a normal CRP level i.e. (<2.5 mg/dl) 12 hours after the onset of symptoms excluded the diagnosis of acute appendicitis[9]. In our study, serum CRP measurements preoperatively were found to be highly sensitive about (98%) in patients with acute appendicitis and was likewise highly specific (87%) in patients who did not have the disease.

We found that leucocyte count was a better laboratory test than CRP values in diagnosing uncomplicated acute appendicitis wherease CRP value was much superior to leucocyte count in reflecting appendiceal perforation or abscess formation. These results are in accordance with earlier reports[10]. Previous and present results suggest that increased leucocyte count is usually the earliest laboratory test to indicate appendiceal inflammation. Only during protracted inflammation are levels of acute-phase reactants such as CRP, increased. The leucocyte count does not, however, increase any more during protracted inflammation such as in case of appendiceal perforation or abscess formation as confirmed in the present study.

The majority of the cases in our study, with an uniflammed appendix at appendectomy were women, as was expected owing to gynaecological disorders which mimic acute appendicitis. In women, the diagnostic accuracy in acute appendicitis is usually as low as 60-70%[10]. In cases of women of childbearing age the results are even less satisfactory with the diagnostic accuracy rate usually less than 60 percent. Recently, laparoscopy was recommended in young women with right lower abdominal pain as it usually gives a precise diagnosis and definitely reduces the rate of negative appendicectomies[10].

CONCLUSION

It was also found in our study that total leucocyte count was a good indicator of acute appendicitis but CRP proved to be far superior in predicting complicated cases like perforation/gangrene or abscess of the appendix. The sensitivity and specificity of serum CRP was 98% and 87.5% respectively with a predictive value (PV) of positive test almost 98% and that negative test in the range of 87.5%. If C-reactive protein can be added to the already existing laboratory tests then the diagnosis of acute appendicitis with clinically suggestive signs can be made with a fair degree of accuracy and as such unnecessary appendicectomies can be avoided (Table II).

TABLE-II THE SPECIFICITY, SENSITIVITY AND THE PREDICTIVE VALUES OF SERUM CRP MEASUREMENT IN THE DIAGNOSIS OF ACUTE APPENDICITIS:

CRP	Histopathology Negative	Histopathology Positive	Total
High	2 (FP)	132 (TP)	134
Normal	14 (TN)	2 (FN)	16
Total	16	134	-

Specificity = TN/TN+FP = 14/14+2 = 14/16=87.5%

Sensitivity = TP/TP+FN = 132/132+2 = 132/134=98.5%

Predictive Value (PV)

Of positive test = TP/TP+FP = 132/132+2=98.5%

Of negative test = TN/TN+FN = 14/14+2=87.5%

(FP=false positive, TP=true positive, TN=true negative, FN=false negative)

REFERENCES

1. Bolton JP, Craven ER, Croft RJ, Menzies-Gow N. An assessment of the value of the white cell coum in the management of suspected acute appendicitis. Br J Surg 1975; 62: 906-8.
2. Gronroos JM, Gronroos P. A fertile-aged woman with right lower abdominal pain but unelevated leucocyte count and C-reactive protein. Acute appendicitis is very unlikely. Langenbecks Arch Surg 1999 Oct;384(5):437-40.
3. Tillet WS, Francis R: Serological reaction in peneumonia with a non-protein somatic fraction of penumococcus. J Exp Med 1`930; 52: 561-571.
4. Pepys MB, Baltz ML. Acute phase proteins with special reference to C-reactive protein and related proteins (pentraxins) and serum amyloid A protein. Adv Immunol 1983; 34: 141-211.
5. Young D.R. Results of Urgent Appendicectomy for Right Lower Quadrant Tenderness. Am. J. Surg., 1989, 157, 428-430.
6. Kragsbjerg P, Holmberg H, Vikerfors T. Serum concerntrations of interleukin-6, tumour necrosis factor and C-reactive protein in patients undergoing major operations. Eur J Surg 1`995; 161: 17-22.
7. Gronroos JM, Gronroos P. Leucocyte count and C-reactive protein in the diagnosis of acute appendicitis. Br J Surg 1999. 86:501-4.
8. Eriksson S, Granstrom L, Carlstrom A. The diagnosis value of repetitive preoperative analyses of C-reactive protein and total leucocyte count in patients with suspected acute appendicitis. Scand J Gastroentereol 29:1145-9.
9. Albu E, Miller BM, Choi Y, et al: Diagnostic value of C-reactive proptrin in acute appendicitis. Dis Colon Rectum 1994 ; 37: 49-51
10. Gronroos JM, Gronroos P. A fertile-aged woman with right lower abdominal pain but unelevated leucocyte count and C-reactive protein. Acute appendicitis is very unlikely. Langenbecks Arch Surg 1999 Oct;384(5):437-40.

FREQUENCY OF MALIGNANT TUMOURS IN CLINICALLY SUSPECTED LESIONS OF ORAL CAVITY

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ABSTRACT:
The objective of the study was to know the histopathological nature of clinically suspected lesions in the oral cavity. It was a descriptive study conducted in the Departments of ENT and Pathology, Jinnah Postgraduate Medical Centre, Karachi from January 2002 to December 2002. A total number of 149 cases, 73 males and 76 females of all ages were selected. Neoplastic lesions were more common (61%) followed by benign lesion (39%).

KEY WORDS: Malignant tumor, Oral cavity

INTRODUCTION

Oral cavity lesions are very common in Pakistan. Most of them are malignant in nature. Late presentation is the major adverse factor noted in the management of these malignant lesions[1]. Benign lesions are also not uncommon. Histopathology is mandatory to reach upon the exact diagnosis. Oral cavity cancer is second most common cancer in Pakistan after carcinoma lung in males and carcinoma breast in females[2].

The incidence of neoplastic diseases has progressively increased during the past 50 years. The actual increase in incidence is due to technologic advances (like new chemicals, radiation, and other factors) and our mode of living which makes it possible to come in contact with carcinogenic agents e.g. significant increase in cigarette smoking, pan chewing, increased intake of preserved food. As there has been increase in the life expectancy above 60 years, so more people are living up to the cancer age (> 50 year)[3]. The purpose of the study was to know the frequency of malignant tumors in clinically suspected lesions of oral cavity.

PATIENTS AND METHODS

This descriptive study was conducted at Institute of Basic Medical Sciences of JPMC in collaboration with Department of ENT, JPMC during the year 2002 focusing on the morphological diagnosis of lesions in the oral cavity. All suspected cases of malignancy of oral lesions are sent to Department of Pathology, Basic Medical Sciences Institute for confirmation. During the period under study (January 2002 to December 2002), 47,252 patients reported at ENT OPD and 230 patients were sent for histopathology. Out of these 230 patients, 149 (64.8%) of oral cavity were included in the study. At the Department of Pathology of BMSI, the oral biopsies received from ENT Department along with prescribed proforma were put in 10% formaline for fixation. The representative section were taken, embedded and processed. The staining was done by routine method i.e. H and E special stains like PAS, trichrome and retic were also required for most of the cases.

RESULTS

Among 149 cases of suspected malignancy of oral cavity sent for histopathology, there were 76 (51%) females and 73 (49%) of males. The mean age of females was 43.6±15.45 years and of males 49.86±15.25. years. The lesion of oral mucosa found in 115 (77.2%) cases followed by that of tongue, 34 (22.8%) cases. Out of 149 cases, 91 (61.0%) were confirmed as malignant. Among these, 80 (87.9 %) were of squamous cell carcinoma, 8 (8.7%) of verrucous, 02 (2.2 %) of un-differentiated tumor and 1 (1.1 %) of adenoid cystic carcinoma. The benign cases were 58 (39.0%). The proportion of malignancy among oral cavity was found statistically significant as compared to benign cases. ($p=0.001$, $X^2 = 14.62$).

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DISCUSSION

Our study of 149 cases of oral cavity biopsies with 91 (61%). malignant cases contributed to 16.1 % of the total malignant cases (564) found during the same study period of one year. The study by Zaidi[2] conducted in 1976 revealed an incidence of 26.4% of all cancers. It shows that recently a decrease in occurrence is noted. Also our rate is almost similar to the study by Burgri[6] in 1995-96 (which revealed 10.9% of all malignancies are those of oral cavity). As regards site of distribution, our study also confirmed tongue and buccal mucosa as the two commonest sites of malignant lesion.

Most of the patients (55%) were between 31-60 years. Study by Hashmi [7] conducted at Multan in 1999 revealed 39% of the patients were between 31-60 years So geographical variation is therefore an important variable. Distribution of histopathology is not different as in other studies Squamous cell carcinoma is the Still commonest followed by others but with minor variation. It is thus concluded that use of betel quads is the most common cause of malignancy in oral cavity followed by smoking and chewing habit. It is recommended that measures should be taken to publicize about the hazards of pan chewing, niswar taking and smoking.

REFERENCES

1. Maren, AGD Stell P M Head and neck surgery. 4th ed. Oxford. Butterworth. 2000 275-317.
2. Zaidi, SH.A monograph on oral cancer Karachi, Royal Book Company 1995.
3. Major M. Oral Pathology, an introduction to general and oral pathology for hygienist 6th ed. Philadelphia, Lea and Febiger 1992.126-127.
4. Dimsbraulis, Oral cancer. A synopsis of pathology and management. Oxford Wright. 1998. 4-5.
5. Cawson RA. Cawson's essential of oral pathology and oral medicine 7th ed. Edinburgh, Churchill Livingstone 2002. 250.
6. Bhurgri Y, Rahim A et al; The pattern of malignancies in Karachi (1995 to 1996) JPMA, 1999, 49:157-161.
7. Hashmi MI, HashmiTHanif MZ, et al Lesion in oral cavity, a hospital based study of etiological correlation with local factors and histological typing. Professional, 1999 6: 201-6.

RESULTS OF DIFFERENT MODES OF MANAGEMENT OF LIVER ABSCESS IN CHILDREN

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ABSTRACT:

Liver abscess is not an uncommon problem in children. Different modes of management are described in literature, but the best one is still controversial The purpose of this study was to compare the results of different modes of management of liver abscesses in children, so as to suggest the most appropriate method of dealing with this condition in sense of early recovery, at minimum cost and with least complications.

This study was carried out on 38 children with liver abscess during one year period, from 1st January 1999 to 31st December 1999 at the National Institute of Child Health, Karachi. Diagnosis was made on history, examination and investigations. Ultrasound and IHA(indirect hemagglutination antibodies) were the main diagnostic tools. Abscesses larger than 5cm.were managed by drainage. Three subgroups were formed. These were; percutaneous needle aspiration, percutaneous tube drainage and drainage by laparotomy. Results were analysed in terms of complications, cost and duration of illness.

All different modes of management remained successful. There was no mortality. Recurrence was noted in one patient in percutaneous needle aspiration, which was managed by second aspiration. Granulation tissue formation was found at site of exit of tube after percutaneous tube drainage in two cases. In open drainage two patients developed excessive bleeding, in three patients contamination of peritoneal cavity occurred during procedure and in one patient fits and septicaemia developed.

It is thus concluded that abscesses more than 5cm (uncomplicated) can successfully be drained by percutaneous needle aspiration under ultrasound guidance. The method was found safe, cost effective and with least complications

KEY WORDS: Liver abscess, Children, Management.

INTRODUCTION

Liver abscess, regarded, generally a rare condition in the Western world, is not an uncommon problem in children residing in tropical countries. Bacterial and parasitic invasion of liver are the two common etiological factors[1]. Clinical features are variable depending upon the cause, size of abscess, general health, the features of associated disease and complications.[2,3]. Among investigations, role of ultrasound in diagnosing liver abscess and role of IHA in diagnosing cause of liver abscess are very important.[4,5,6] Treatment of patient is either medical or surgical, depending upon the size, location, toxicity and response to antimicrobials. Surgical procedure depends upon surgeon's previous experience and facilities available. The best mode of management is controversial. The purpose of this study was to compare the results of different modes of management of liver abscesses in children so that a cost effective method, with least morbidity can be recommended.

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PATIENTS AND METHODS

Thirty eight cases of liver abscess were managed in this study during one year period at the National Institute of Child Health, Karachi. Complete history was taken and

examination was carried out. Ultrasound and Indirect haemaglutination test were the main diagnostic tools. IHA titer above 250 was taken positive for amoebic liver abscess. All the cases negative for IHA were included in pyogenic group whether pyogenic organism was seen or not.

For management two groups were made. In the 1st group, abscess smaller than 5cm were managed conservatively and 2nd group abscess larger than 5cm were managed by drainage. Second group was again divided into three sub-groups. (a). drained by percutaneous needle aspiration under ultrasound guidance (b) drained by passing tube percutaneously after demarcation with ultrasound (c) drained by open surgical procedure.
Results were analyzed in term of complications, cost and duration of illness.

If recurrence occurred after aspiration there is no harm in doing a second aspiration. Initially both amoebicidal and antibiotics were started. As IHA report became available and was negative amoebicidal was stopped and antibiotics continued for four weeks. If IHA was found positive, antibiotics were given for 2 weeks only, to cover superadded infection and amoebicidal drugs continued for four weeks

RESULTS

Thirty eight children were managed in this study. Youngest child was 1½ year old and the oldest was 12 years, average age was 5.5 years. Most children were between 4-7 years of age. Thirty patients were male and 8 were female. Male to female ratio is 3.75:1.

History of dysentery was present in 7 cases (18 42%). On examination malnutrition, anemia and tender hepatomegaly were common findings. Respiratory distress was seen in two patients with liver abscess that had ruptured into the thoracic cavity. Hemoglobin was found low (<l0g%) in 32 cases (84.21%). TLC count was raised in 16 patients (42.10%). IHA was done in 24 cases. It was positive in 18 cases (75%). Pus culture was done in 2l cases and bacterial culture was found positive in 5 cases (23.80%). In 2 cases it was Staphylococcus aureus and Pseudomonas was found in 2 cases. Stool DR was done in 15 cases and Entamoeba histolytica was not seen in any case. X-ray abdomen was done in 21 patients. Elevation of diaphragm was the most common finding and was seen in 14 cases (66.66%). Other findings included increased soft tissue shadow of liver and pleural effusion. Single abscess in right lobe of the liver was the commonest finding on ultrasound. Six patients had abscess smaller than 5cm and 32 patients had abscess larger than 5cm. Colour of pus was found yellow in 22 cases (66.75%), anchovy sauce in 8 cases (25%) and yellowish green in 2 cases (6.25%).

Six patients with abscess <5cm were managed by conservative means. Fever settled in average 8 days, no complication was seen. Abscess cavity resolved in average 30 days. Out of 32 patients with abscess larger than 5cm, 10 patients were managed by percutaneous needle aspiration under ultrasound guidance, 10 cases by passing percutaneous tube after demarcation with ultrasound, 10 cases by open surgical drainage. 2 cases who had abscess ruptured into the pleural cavity were managed by tube thoracostomy only.

In percutaneous needle aspiration only local anaesthesia was required with almost no blood loss. Blood transfusion was needed in 50% of cases because of pre-existing anemia. No major complication was seen. Recurrence was noted in one case that was managed by second aspiration. Fever settled in average 7 days and stay was average 7 days. The cavity resolved in average 25 days.

In percutaneous tube drainage, local anaesthesia was required, blood loss was less than 5cc. 80% of cases needed blood transfusion (mostly because of pre-existing anemia). No major complication was seen. Excessive granulation tissue formation was seen at the site of tube in two cases Average hospitalization was 7 days and the cavity resolved in average 30 days.

In open surgical drainage general anaesthesia was required, operation theatre and more manpower was needed. Blood transfusion was given to all patients. Per operatively excessive blood loss was seen in two cases, contamination of peritoneal cavity accurse in 3 cases, wound infection seen in two cases, septicaemia and fits in one case. Fever settled in average 5 days. No recurrence was seen. Average hospitalization was 7 days and cavity resolved in 40 days.

For tube thoracostomy in cases of liver abscess that had ruptured into the pleural cavity, local anaesthesia was required. No major complication was seen. Fever took longer time to settle (average 20 days), duration of hospitalization was average 30 days and abscess cavity resolved in average 130 days. No recurrence was seen.

DISCUSSION

Liver abscess is not an uncommon problem. Fever RUQ pain and vomiting were common presenting features. Amoebic liver abscess is more common than pyogenic. Single abscess in right lobe is more common. Ultrasound is highly diagnostic.[3] Most patients had low haemoglobin, leucocyte count may be normal because it depends upon patient's immunological status.[9] Microscopic examination of pus was not found to be much helpful for diagnosing the cause. Elevated right dome of diaphragm was common x-rays finding. Colour of pus was anchovy sauce like only in 8 cases, while number of amoebic liver

abscess was much higher, this may be because of superadded infection by pyogenic organism.

In our study non-operative management of smaller abscess (>5m) was the best, as it was of low cost and patients can be managed in outpatient department. There are few demerits of this procedure as thick pus is sometimes difficult to drain, fever takes longer time to settle, more chances of recurrence.

Percutaneous needle aspiration under ultrasound guidance was found best for non-complicated larger abscess (>5cm) as also proved by other studies.[9,10] It is easy and safe procedure, hepatic trauma is minimal and chances of bleeding are very low. There are few demerits of this procedure as thick pus is sometimes difficult to drain, fever takes .longer time to settle. There are more chances of recurrence.

Percutaneous tube drainage after demarcation with ultrasound has advantage that thick pus can also be drained, hospital stay is short and there is early recovery. Its disadvantages are that it is a relatively blind procedure. The chances of hepatic damage, bleeding, perforation of diaphragm, empyema and bronchopulmonary fistula are more. The approach for abscess present in the posterosuperior aspect of right lobe of liver is difficult.

Open surgical procedure drainage has advantage of proper drainage of pus accompanied with thick slough, a short hospital stay and early recovery. Among its demerits include general anaesthesia, it is a major surgical procedure with more chances of blood loss, contamination of peritoneal cavity and wound infection.

Tube thoracostomy is a safe procedure for ruptured liver abscess into the pleural cavity, though duration of hospitalization, time required for fever to settle and the abscess cavity to resolve is more. Fever takes longer time to settle after percutaneous needle aspiration, so just persistence of fever is not the only indicator of failure of procedure or justification for laparotomy. After drainage of pus, the cavity takes longer time to resolve. Hence presence of cavity on follow up ultrasound sometimes is confused with persistence or recurrence of abscess.

REFERENCES

1. Mehnaz A, Mohsin S: Liver abscess in children not an uncommon problem. Pakistan Medical Association JPMA, 1991; -273-5.
2. Noons, Milar MW: Liver abscess in childhood, Pediatr Surg. int. 1988; 3: 27-32
3. Ranairez CP, Hernandex H Jauri H Ameobic hepatic abscess in children. J. Pediatr. Surg. 1995-30, -662-4.
4. Memon A.M., Memon J.M.: "Liver abscess in children J. Surg. Pakistan (International) 1997 2; -13.
5. Gulshan Au, Qayyum M.A, Ali Mr. An experience with amoebic liver abscess at PMCH Nawab Shah Medical Channel, 1999 2 ; 1-14.
6. Nur ul Amin M: Amoebic liver abscess review article, Specialist, Pakistan Med. Soc, 1997, 13 :279-292; .
7. Moazam F, Nazir Z: Amoebic liver abscess "Spare the knife but save the child". Karachi Pakistan. J Pediatr Surg. 1998 33; 199-202.
8. Touloukin JR: Non malignant liver tumours and hepatic infections. Textbook of Paed. Surgery 4th: 1986, 2; -1071'
9. Mustafa A, Safdar AM: Liver abscess presentations and management mother and child 1997 35. 67-69.
10. Samo MJ, Ahmed M Aspiration of liver abscess. Pak J. Med Sciences; 1997, -13 389-392.
11. George W, Hol Comb , John B: Gall bladder disease and hepatic infections. Textbook of Paediatric Surgery 2: 502.

INCIDENTAL DIAGNOSIS OF EARLY CARCINOMA GALL BLADDER IN CHRONIC CHOLECYSTITS WITH CHOLELITHIASIS

MAZHAR IQBAL, KHALID RASHID, ZIA UL ISLAM, ASADULLAH KHAN

ABSTRACT:
The objective of this study was to find out the number of incidental early carcinoma gall bladder in chronic cholecystitis with gall stones and to evaluate the age and sex distribution of early carcinoma of gall bladder in our set up. The study was conducted in ward 3 Jinnah postgraduate Medical Centre Karachi for five years from January 1997 to December 2001.

A total 604 Patients diagnosed as chronic cholecystitis with gall stones in surgical out patients department, were admitted in ward 3 after carrying out all the necessary investigations for gall stones disease and underwent cholecystectomy. Histopathology was done at The Basic Medical Sciences Institute Jinnah Postgraduate Medical Centre Karachi, and in 24 patients we incidentally found on histopathological report, an early carcinoma gallbladder.

Incidental diagnosis of carcinoma gall bladder with gall stones in our study was 3.97%. Carcinoma gall bladder was more common in females (91.67%). Male to female ratio was 1: 11. and more common around 50 years of age. Incidental diagnosis of carcinoma gall bladder with gall stones is very high in our setup (3.97%) and relatively in younger age (41 to 60 years) group in our study. The role of early cholecystectomy to prevent and cure carcinoma gall bladder in early stages is essential even silent stones should not be ignored.

KEY WORDS: Cholelithiasis, Gall Stones, Carcinoma gall bladder.

INTRODUCTION

Carcinoma gall bladder is the most common cancer of biliary tract. In 60 to 90% of cases gall stones are also present[1]. Females are affected more than males[2], most often in 70 to 75 years of age[1]. Aetiology of carcinoma gall bladder is unknown. Several risk factors are associated with the disease, some of them are gall stones, carcinogen, porcelain gall bladder, typhoid carrier, gall bladder polyp, adenomyomatous anomalous pancreatico biliary duct junction, oestrogen , choledochal cyst and bacteria in bile,[3,4,5,6,7,8].

Gall stones may cause epithelial dysplasia, a typical hyperplasia and carcinoma in situ[1]. Most cancers of gall bladder are adenocarcinomas and some are mucin secreting. These grow either in infiltrative pattern or as exophytic lesion fungating into the lumen. All spread by local expansion and direct permeation of liver is characteristics of those that arise in the liver bed of the gall bladder. Many situated near the neck of gall bladder produced symptoms, highly reminiscent of gall stones. Those arising in the fundus of gall bladder remain silent until metastasis occurs[1].

Patient's symptom may be indistinguishable from those of cholecystitis. In the remaining cases disease is entirely occult. In some cases anorexia and weight loss are the only presenting complaints[1]. More frequent use of cholecystectomy seems to he the best prevention of carcinoma gall bladder in any case of cholelithiasis whether symptomatic or not in the absence of any contraindication[9,10]. Five years survival rate for all the gall bladder cancer in most series is 0-10%[2]. This poor prognosis is due to the special anatomical situation of the gall bladder and late cholecystectomy for gall stones[6].

Aims of our study were to find out incidental cases of early carcinoma gall bladder in chronic cholecystitis with gall

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stones and to evaluate age and sex distribution of early carcinoma gall bladder (which is confined to gall bladder wall) in our setup.

PATIENTS AND METHODS

This study was carried out in ward 3 of Jinnah Postgraduate Medical Centre Karachi, from January 1997 to December 2001 for the period of five years. All the patients were admitted through surgical out patient department after necessary investigations. All patients who were initially diagnosed as chronic case of cholecystitis with gall stones and later on histopathology report proved carcinoma gall bladder, were included in the study. No Preoperative diagnosis of carcinoma gallbladder was not made in any of these cases. All the patients who were diagnosed on clinical examination or those with a suspicion of carcinoma gall bladder on ultrasonography and with evidence of metastasis were excluded from the study.

All the patients with diagnosis of chronic cholecystitis underwent cholecystectomy and gall bladder specimens histopathological examination was done at the Basic Medical Sciences Institute Jinnah Postgraduate Medical Centre Karachi, and final diagnosis was made on histopathological report.

RESULTS

During the period of study a total 604 patients underwent cholecystectomy and histopathology of all the gall bladder removed was carried out. Twenty four patient (3.97%) were reported as having adenocarcinoma of gall bladder. Early carcinoma gall bladder was more common in females in our study (n=22). Even a younger age group was involved in carcinoma gall bladder. Male to female was I:II Age distribution is given in Table I.

TABLE-I AGE DISTRIBUTION

Age in years	No. of Patients with Carcinoma Gall Bladder	Percentage
30 – 40	3	12.5%
41 – 50	10	41.66%
51 – 60	7	29.17%
61 – 75	4	16.67%

DISCUSSION

In our study 3.97% patients of gall stones who underwent cholecystectomy proved to have carcinoma gall bladder. Carcinoma gall bladder was observed in 3.2% patients in a study conducted in three major hospitals located in the Northern area of Melbourn[6]. As compared to this study the incidental diagnosis of early carcinoma gall bladder in our setup is slightly higher. The delay in cholecystectomy predisposes the mucosa to metaplasia leading to carcinoma of gall bladder[6]. The cause of delay of operation in our setup is avoidance of operations by patients due to poverty and overload of patients in our surgical out patients department especially when they are symptom free. Other reasons may be the cost, ignorance and fear of operations. The long standing benign gall stones disease of may results in carcinoma gall bladder. In our study male to female ratio was 1:11 as compared to other study in which ratio was 5:1[8]. The oestrogen causes stasis and gall stones formation which predisposes to carcinoma gall bladder in female. In our study carcinoma gall bladder was more common in females, similar to other studies but the percentage is slightly higher. The other important aspect of our study was that carcinoma gall bladder are more common in 40-60 years of age but in other studies common age group involved was 60-75 years of age[11]. As compared to other studies, 12.5% younger patients (30-40 years of age) proved to be carcinoma gall bladder in our study and no congenital abnormalities of gall bladder was found in these patients. Thus gall stones may be the only aetiological factor. Other predisposing factors like porcelain gall bladder, typhoid carrier, gall bladder polyp were not found in our study.

Incidental diagnosis of early carcinoma gall bladder in our study was higher as compared to other studies. So early cholecystectomy can prevent or cure the early carcinoma gall bladder. Gall stones have strong association with carcinoma gall bladder. As compared to other studies relatively younger age group was involved in our study so some environmental factors may be the cause of carcinoma gall bladder (like dietary factor).

REFERENCES

1. Kumar , Smith. Carcinoma of Gall Bladder. Basic pathology 1992 5th edition:565-66
2. Parkash O. On the relationship of cholelithiasis to carcinoma of gall bladder and on the sex dependency of the carcinoma of the bile ducts. A study based on the autopsy data from 1921 to 1972. Digestion 1975 12:129-33
3. Scott TE, Carrol M, Cogliano FD, Smith BF, Lamorte WW. A case control assessment of risk factors for gall bladder carcinoma. Dig Dis Sci 1999 44:1619-25
4. Mirsa N.G, Mirsa S, Chaturvedi A. Carcinoma of Gall Bladder. Recent advances in Surgery 1997 -20:69-11
5. Csendes A, Becerra M, Burdiles P, Banalari K, Csendes P. Bacteriological studies of bile from the gall bladder in patients with carcinoma of Gall bladder, cholelithiasis, common bile ducts s and no gall disease. Eur J Sur 1994 160:363-7
6. Nair HT, Hirve SS, Pikale HS, Shenoy SG. Anomalous presentation of a case of carcinoma of the gall bladder with Gall stones. J Postgrad Med 1917 Jan 33:32-3
7. Shukla VK, Tiwari SC, Roy SK. Biliary bile acids in cholelithiasis and carcinoma of the gall bladder. Eur J Cancer Pre 1993 2:155-60

8. Vitetta L, Sali A, Little P, Mrazek L. Gall Stones and gall bladder carcinoma. Aust N Z J Surg. 2000 Sp 70:667-73

9. Henery X, de Lestagnge – Labrocesse M, Stoppa R, Banti BJ. Primary cancer of Gall bladder, proposal of preventive approach. J Chir (Paris) 1977.113-94

10. Korean K, Fabian F, Horvath A, Chylo E, Waltzer I, Filipek P, et.al. The importance of early cholecystectomy in cholelithiasis for the prevention of Carcinoma of the gall bladder. Bratisl Lek Listy 1919 June 90:416-21

11. RCG . Russell, N.S Williams, C.J Bulstrode. Carcinoma of Gall bladder Bailey and Love 23rd edition, 2000 -986

SPINAL ANAESTHESIA FOR CAESAREAN SECTION: A COMPARISON OF ISOBARIC AND HYPERBARIC SOLUTIONS OF 0.5% BUPIVACAINE

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ABSTRACT:

The objective of this study was to compare the effect of barricity of 0.5% bupivacaine in spinal anaesthesia for caesarean section. It was conducted at the Department of Anaesthesia, Hamdard College of Medicine and Dentistry, Karachi between January 2002 to December 2002. It was a randomized double blind clinical trial.

Fifty ASA I patients were given spinal anaesthesia with 2.5ml. of 0.5% bupivacaine for caesarean section. Except for barricity of the solutions injected, identical technique was used for every parturient in the study. The solutions were 0.5% bupivacaine isobaric and 0.5% bupivacaine in 7.5% glucose (i.e. hyperbaric) and accordingly the patients were divided into two groups I and II and comparison was made in respect of sensory, motor and cardiovascular effects. Both isobaric and hyperbaric solutions given in lateral position produced adequate analgesic levels. The only difference between the two was that the onset of sensory block was quicker with isobaric solution and onset of motor block was earlier with hyperbaric bupivacaine and the sensory effect lasted longer in isobaric group. Motor block also lasted longer in isobaric group. However hyperbaric bupivacaine solution produced higher haemodynamic changes and subjective feeling of 'feeling sick' than isobaric bupivacaine, but these too were not statistically significant. Our results indicated that the anaesthetic effect was adequate in both study groups but each group had some advantage over the other. Therefore use of any particular bupivacaine for caesarean section, hyperbaric or isobaric can be done on individual preference and availability.

KEY WORDS: Caesarean Section, Spinal anaesthesia, Bupivacaine, Isobaric, Hperbaric.

INTRODUCTION

Spinal anesthesia for caesarean section avoids maternal and fetal risks of general anaesthesia, therefore it is the preferred technique. Virtually all local anesthetics used for spinal anesthesia are available as hyperbaric solutions and it is well established that the addition of dextrose to increase the specific gravity of a solution alters the anesthetic profile of the drug[1]. The present study was undertaken to compare the outcome of isobaric versus hyperbaric bupivacaine solutions in lateral position, a technique simulating our routine practice. The solutions used were bupivacaine 0.5% plain or mixed with 7.5% glucose.

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SUBJECTS AND METHODS

Following institutional approval and informed patient consent 50 uncomplicated full term parturients undergoing elective caesarean section for whom spinal anesthesia was considered appropriate were enrolled for the study in a randomized manner. The parturients were divided into two groups of 25 each. Patients in group I received 2.5 ml. of 0.5% bupivacaine plain (isobaric), while those in group II received 0.5% bupivacaine with 8% dextrose 2.5ml. The solutions used were available in ampules of 10ml and 4ml. respectively. The patients were not given any premedication. In the operating room the pulse and blood pressure of patients were recorded in the

supine position and 500ml of lactated ringers solution was infused in 15-20 minutes. Each patient was then laid in left lateral position . Under all aseptic precautions a 24 guage spinal needle was inserted in L2-3 or L3-4 space through midline approach. The anaesthetic solution was injected without barbotage or aspiration at the end of injection. Immediately after injection the patient was assisted and made to lie in the supine position. A wedge was not used as it is not the standard practice in our setup. Cephalad spread of analgesia was assessed by loss of sensation to pin prick and motor blockade was determined according to criteria in Table II and III respectively. Both sensory and motor blockade were determined at 2 minute intervals for the first 20 minutes and then every 15 minutes until full recovery. The observer as well as the parturients were blinded to the anesthetic solutions used. The haemodynamic changes were monitored every 2 minutes for the first 20 minutes and then every 5 minutes till the completion of surgery. No sedation was given after delivery of the baby.

RESULTS

Total number of patients in this series was 50 (Table. I). All patients developed adequate anesthesia for caesarean section. The median highest sensory level was T4 in group I and T6 in group II. The time from injection to sensory blockade till T10 was 3.39 and 3.48minutes in I and II groups respectively, and mean time taken for highest level was 12.28 in group I and 14.28 in II group. The mean regression time to T10 was 188 minutes and 174 minutes in I and II groups respectively and the mean regression time to S1 level was respectively 239 and 208 minutes in group I and II. (Table II).

TABLE-I PATIENT CHARACTERISTICS

	Group I n-25	Group II n-25
AGE (years) Mean	22.5	21
RANGE	(18-34)	(17-32)
WEIGHT (kg) Mean	68	71
RANGE	(56-98)	(58-94)
HEIGHT (cm) mean	157	156
RANGE	(154-168)	(155-166)

TABLE-II ASSESSMENT OF SENSORY BLOCK

Group	Time To T 10	Time To Highest Level	To Regression Time	S1 Regression Time
Sensory Block				
I	3.39 Minutes	12.28 Minutes	188 Minutes	239 Minutes
II	3.48 Minutes	14.28 Minutes	174 Minutes	208 Minutes

The mean time to motor blockade of grade 1(as in table III), that is onset of motor block was 6.24 minutes and 4.12 minutes respectively in I and II groups. The mean time taken to complete the motor block to grade 3 (table III) was 12.22 minutes in group I and 10.13 minutes in group II. The mean return of muscle power to zero grade (Table III) was 218.90 minutes in group I and 187.5 minutes in group II. The results of motor block are also tabulated in Table IV.

There was no statistical difference in the two groups as far as onset and completion of motor block is concerned but the return of complete muscle power to zero was statistically different in I and II groups (p .01). Blood pressure drop was more in group II as compared to I, but not statistically significant (Table V). But the maximum heart rate change was similar in both the groups. Nausea and subjective sensation of feeling sick was observed in 12 patients in group II and only 4 patients in group I. Post spinal headache was not seen in any patient.

TABLE-III MOTOR BLOCKADE: CRITERIA FOR ASSESSMENT

0	No Motor Block
1	Unable to raise Leg & Knee extended
2	Unable to Flex Knee
3	Unable to dorsiflex ankle

TABLE-IV MOTOR BLOCKADE

Group	Onset to Grade 1	Completion Grade 3	Motor Block Regression to Grade 0
Motor Block			
I	6.24 Minutes	12.22 Minutes	218.9 Minutes
II	4.12 Minutes	10.13 Minutes	187.5 Minutes

TABLE-V HAEMODYNAMIC CHANGES

	Group I	Group II
Max Fall in MAP	14 mm of Hg	32 mm of Hg
No. of Patients Dropping MAP	19 mm of Hg	26 mm of Hg
Bradycardia (Mean Max. Fall)	9.5 beats/minute	9.8 beats/minute

DISCUSSION

The anesthetic technique for caesarean section can be general anesthesia or regional. General anesthesia is optimal for emergency situations and substitutes for regional anesthesia when regional is contraindicated. Nevertheless general anesthesia does have a number of disadvantages. Sometimes even in the most experienced hands airway management and adequate ventilation

becomes difficult[1]. Therefore employing regional anesthesia for caesarean section avoids both maternal as well as foetal risks, and is the preferred technique.

Epidural anesthesia is excellent if there is an indwelling epidural cannula during labour. But in elective caesareans spinal anesthesia is superior to epidural as it is easy to perform, consumes less time and has a higher success rate and causes less trauma to tissues[2]. Bupivacaine is the most popular drug especially in teaching hospitals because of its sufficient duration of action. It is not logical to compare the subarachnoid spread of two anesthetic solutions of different barricities when given in sitting position (more caudad spread being heavy), therefore lateral position was preferred and so also because it is our routine practice too, especially in obstetric patients.

Regardless of barricity of the anesthetic solution used the volume of local anesthetic administered into the subarachnoid space is the primary determinant of drug spread due to simple 'bulk displacement' or area contact[3]. A large volume will have a greater spread and effect more spinal segments than will a smaller volume. In our study we used the maximum recommended volume in obstetric patients and also we used the same volume that is 2.5ml. in all patients to maintain uniformity. The concentration used was 0.5% as 0.75% bupivacaine does not give any added advantage in the sensory and motor effects but causes more complications[5]

As we gave the drug in left lateral position to all patients we achieved nearly similar dermatome sensory blockade in both I and II groups. In sitting position hyperbaric drug tends to settle down with gravity and lower dermatome level of anaesthesia is produced than isobaric or hypobaric solution due to dependant spread[4]. Also hyperbarric solutions tend to cause sacral pooling which causes more urinary retension. We are not able to make a comment on urinary retension in our study as all patients had indwelling urinary catheters.

Post spinal headache has been reported in many studies,[5,6] but we did not have headache even in a single patient. We found that the onset of sensory block was quicker in group I ($p<0.001$) and time to highest peak level also was shorter in group I ($p<0.001$) than in group II. Similar results have been obtained in the study of King et al. But regression of sensory block was delayed in isobaric group as compared with hyperbaric grouping our study which was not so in Kings study.

The difference in the onset time of sensory block in between the two groups had no advantage in elective caesarean .However in emergency caesarean section this would be advantageous. The delayed recovery from sensory block however would be advantageous as patients would remain pain free for a longer time in group I.

Various studies have obtained variable results. Russel and Holmquist did not obtain any difference in the rate of onset, maximum spread and incidence of post spinal headache when they compared isobaric with hyperbaric 0.5% bupivacaine solutions given for caesarean sections[9].

Motor block was quicker in onset ($p<0.001$) and completion to grade three ($p<0.001$) in hyperbaric than isobaric grouping our study, and recovery to grade zero was also faster in this group ($p<0.001$)This complies with the study of Axelson et al[10].

Thus our study results show advantages with 0.5% bupivacaine plain regarding sensory block and 0.5% bupivacaine heavy regarding motor block. Our results and variable results of many other studies[2] indicate that despite its long history and popularity some of the factors that affect spinal anesthesia still remain controversial and unveiled.

There are too many variables involved in predicting the outcome of spinal anesthesia . Alteration in drug parameters, technique, as well as individual patient factors may singly or collectively produce different results. Practice of spinal anesthesia can thus be done with variable drug barricities, depending on availability in any particular institution without much to gain or loss at patients end.

REFERENCES

1. King HK, AshleyS, Brathwaite D,Decayette J, Wooten DJ,:Adequacy of general anaesthesia for caesarean section. Anaes Analg 1993 77:84-88.
2. King HK,Wood LM, Steffens Z, Johnson C: Spinal Anaesthesia for caesarean section: Isobaric versus Hyperbaric solution.Acta Anaesthesiol,SIN 1999 37;61-64.
3. Riley ET, Cohen SE, Macario A, Desai JB, Ratner Ef: Spinal versus epidural anesthesia for caesarean section: a comparisiom of time efficiency, costs, changes and complications. Anesthesia & Analgesia 80: 1995 709-712.
4. King HK. Factors influencing subarachnoid block. Progress in Anaesthsiology 20:45-49,1995.
5. Chambers WA, Littlewood DG, Edstorm HH, Scott DM: Spinal anesthesia with hyperbaric bupivacaine: effects of concentration and volume administered. 175-180, 1982 BJA 54(1):
6. Alston RP, Littlewood DG, Meek R,Edstrom HH. Spinal Anaesthesia with hyperbaric bupivacaine: Effects of concentration and volume when administered in sitting position . BJA. 1988 61: 144-148.

7. Chambers WA, Elstrom HHScott DB. Spinal Anaesthesia with 0.5% bupivacaine 3ml: comparison of plain and hyperbaric solutions administered to seated patients. Br J Anesthesia. 1981. 53;279-282,

8. Saxena KN, Dua CK.Subarachnoid block :A comparison of Isobaric and hyperbaric solutions of bupivacaine . Ind J Anaesth 1994.42; 246,

9. Russel IF, Holmquist EL: Subarachnoid analgesia for caesarean section: a double blind comparision of plain and hyperbaric 0.5% bupivacaine. 1987 BJA 59: 347-53,

10. Axelson KH, widman GB, Sundberg Ae and Hallgers:A double blind study of motor blockade in the lower limbs. Studies during spinal anesthesia with hyperbaric and glucose-free 0.5 % bupivacaine. 1985 BJA 57(10): 960-970.

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ANTI-SMOKING SCENARIO IN PAKISTAN

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ABDUL RAUF LAGHARI, MASOOD AHMED MUJAHID AKBAR MAMOON

31st May is celebrated as "No Tobacco Day" in whole of the world[1]. This reminds people of adopting good healthy habits especially excluding/extinguishing the established addictive and hazardous habit of cigarette smoking. In the recent years, although a positive, healthy thinking against smoking has been noted / emerged in masses of educated Pakistani people but still a lot should be thought and done at national level.

Arranging few antismoking walks in some big cities in the name of a campaign create no or meager impact on the people of a country, where 70% of the population lives in the rural areas and is not even up to primary education level. With the result nothing could be scored so far by these futile and non-productive efforts.

Tobacco smoking is an important health issue in whole of the world including Pakistan and other underdeveloped countries[2]. There are the countries, where the living conditions are such that no assistance is available for keeping the people's health status sufficient enough to antagonize the harmful effects of this invasive and hazardous habit. The harmfulness can be estimated from the fact that a big school of thought (of medical scientists) has been asking for its (smoker/non-smoker) inclusion as an important vital sign in medicines[3]. This is only because of the various data collected over years which proved that tobacco intake is one of the major most cause of many serious diseases. The cigarettes are available and sold to the customers without looking at their age. The irony touches peak when the salesman himself is usually a teenager. Despite of the availability of the effective methods (that can help a smoker to say good by to this habit) in the 21st century, hardly anyone is available and practiced in our country.

The methods[4,5,6,7] of nicotine replacement therapy (NRT), like n.gums, patch, nasal sprays and inhalers are under practice since eightees . Its use is based on the principle of providing an alternative. This is actually meant to help the patient when coping with the withdrawal effects of stopping smoking and then discontinuing it after few weeks. Last but not the least and a fairly good, no cost method is counseling of the patient. However, this is usually not practiced due to its less effectiveness. It has been observed by consulting a number of doctors of different cities that most were having their own doubts and reservations about their role in counseling the patients against smoking. Although they know that the basis of tobacco smoking is only nicotine addiction[4,8] and this has become a serious health problem in the country, significant barriers exist that interfere with doctors assessment and counseling for treatment. Many of the doctors especially GPs even do not feel it important and necessary to get the basic knowledge of identification of smokers quickly and easily. They hardly have any idea of the available treatment lines and the role of antismoke clinics in the countries.

What needed presently is, to deliver the "Tobacco cessation" help throughout the rural and urban areas of the country. National guidelines and strategic measures must be evolved to fight this menace.[8] At government level atleast, the attractive advertisements in media should effectively be discouraged. This will certainly reduce the monetary load being borne by the health authorities for combating these diseases. We believe this load on government is much much more than the collected taxes from the cigarette selling companies, which are selling this poison to our youth and making their own progress by leaps and bounds. In conclusion, it is vitally important that smoking cessation should be programmed in a scientific way and an integrated system is needed to be devised at primary health care level in the rural are up to tertiary care centers in the cities.

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REFERENCES

1. World Health Organization (WHO) World No Tobacco Day, 31st May 1998. GENEVA: WHO, 1998.
2. World Health Organization (WHO) Tobacco or health; a global status report. Geneva: WHO, 1997.
3. Robinson M, Laurent S, Little J. Including smoking status as a new vital sign: it works. J Fam Pract 1995; 40: 556-63.

4. Godfrey Fowler OBE; Helping Patients to stop smoking (Symposium) "The Practioner", 2002-246, 41-43.

5. Tang J, Law M, Wald N. How effective is nicotine replacement therapy in helping people to stop smoking?. BMJ 1994; 308: 21-6.

6. White A, Resech K, Ernst E. A meta analysis of acupuncture techniques for smoking cessation. Tob Control 1999; 8: 393-7.

7. Houghes JR, Gold stein MG, Hurt RD and Shiffmans. Recent advances in the Pharmacotherapy of smoking. JAMA 1999; 281: 72-6.

8. Raw M, McNeill A, West R. Smoking Cessation guidelines for health professionals. Thorax 1998; 53(Supp 5, Part I): S 3-7.

AN OVARIAN ECTOPIC PREGNANCY

CASE REPORT

ROZINA MUSTAFA

ABSTRACT:
Ovarian pregnancy is a rare form of ectopic pregnancy. Here we report one such case that was managed by laparotomy.

Key words: *Ectopic Pregnancy, Ovarian.*

INTRODUCTION

In ectopic pregnancy the fertilized ovum implants on any tissue other than endometrial lining of uterus. Ovarian ectopic is a rare variant of ectopic implantation. Its incidence has been variously reported as 1 in 7000 to 1 in 60,000 [1].

CASE REPORT

A 25 years old lady, married for the last 5 years was gravida 3, para 1, abortion 1. She was admitted with gestational amenorrhoea of 6 weeks and lower abdominal pain for 3 days. Initially pain was dull in character, but after coitus on the same day of admission, it increased in intensity, associated with shoulder tip pain. On general physical examination she was pale looking. Her pulse was 104/ min, respiratory rate 22/min, blood pressure 90/60 mm Hg and temperature 98 °F. On abdominal examination, guarding and rigidity was present in whole of abdomen more in left iliac fossa. Vaginal examination was not performed.

On admission, her β.HCG was 4985 miu/ml, and ultrasound showed empty uterus with fluid in pelvis including pouch of Douglas and hepatorenal angle. (Figure I a, b).

Patient was managed by laparotomy. Approximately 500-700 cc of clotted and fresh blood was removed. Operative findings showed normal uterus, both fallopian tubes and right ovary. Left ovary was ruptured at its superior surface. Ectopic pregnancy was dissected out from ovary with sharp and blunt curette and specimen was saved for histopathology. Ovary was reconstructed after securing haemostasis. Her post-operative recovery was uneventful. Histopathology report showed decidua with trophoblastic proliferation.

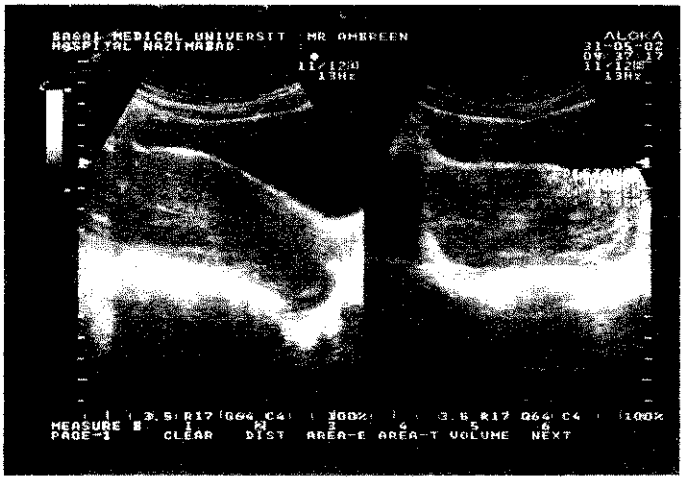

Figure-I a: Ultrasound showing fluid in pelvis.

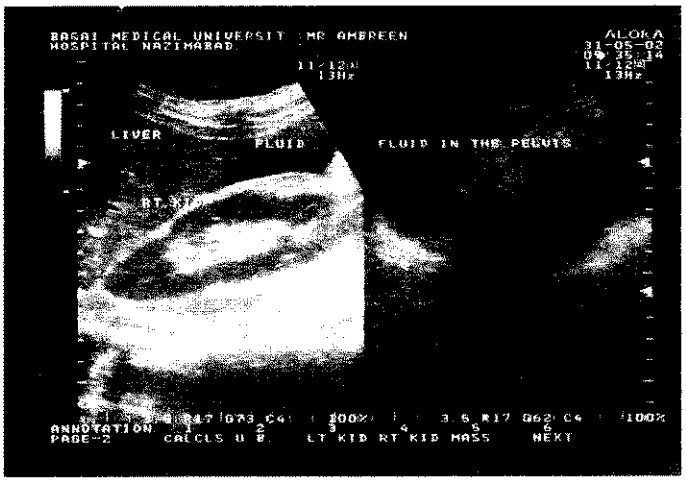

Figure-I b: Ultrasound showing fluid in pelvis.

DISCUSSION:

The diagnosis of an ovarian ectopic pregnancy is seldom made before surgery. At the time of surgery, it is diagnosed when a haemorrhagic mass is seen attached to one of the ovaries in the presence of normal looking

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fallopian tubes. Even then it can be mistaken for haemorrhagic corpus leutum or ovarian cyst[2]. This problem has to a great extent been overcome by availability of serum HCG. A level of 1500 iu/ml in the absence of an intra-uterine sac is highly suggestive of an ectopic pregnancy[1].

Ovary can accommodate more readily than fallopian tube to the expanding pregnancy, though rupture of an ovarian pregnancy is more common at early gestation, often mistaken as ruptured corpus leutum[3] . Spielberg in 1878 put forward four criteria of ovarian pregnancy as :

i) Tube of the affected side must remain intact,

ii) Fetal sac must occupy the position of the ovary,

iii) Ovary must be connected to the uterus by ovarian ligament,

iv) Definite ovarian tissue must be found in sac wall[4] all the criteria was fulfilled by this patient.

Ovarian ectopic pregnancy has same risk factor as tubal pregnancy. This patient during 5 years of her marital life, had one alive child and one induced abortion. She was using on and off emergency contraception for the last one year. Progesterone containing emergency contraception, tablets decreases tubal motility and ciliary movements resulting in delayed movement of fertilized ovum, causing tubal ectopic pregnancy. Ovarian pregnancy can be primary or secondary due to tubal pregnancy abortion. However it is difficult to justify between the two, unlike tubal ectopic which has a significant risk of recurrence, to date there have been no reports of a repeat ovarian pregnancy.[3]

REFERENCES

1. Hallat J. Primary Ovarian Pregnancy. A report of twenty five cases. Am J Obstet Gynecol 1982; 143:50-60
2. Nadarajah S., Sim LN, Loh SF; Case report of laparoscopic management of an ovarian pregnancy. Singapore Med J 2002. 43 : 95-96
3. Nicholls RR, Ovarian pregnancy with living child and mother. Am J Obstet Gynaecol 1941; 42:341-2
4. Spielberg O. Zur Cauistik Der Ovarial Schwanger Schaft. Arch F Gynak 1878; 13:73.

MEGA MUCOCELE OF THE APPENDIX

CASE REPORT

AIJAZ AHMED MEMON, PIR SAHIB SHAH,

ABDUL GHAFFAR ANSARI, ALI AKBER GHUMRO

ABSTRACT:
A rare case of giant mucocele of the appendix found in a middle aged man is reported. Clinically there was a tender, slightly mobile mass in the right side of the abdomen but the ultrasound report was of localized collection in right paraumbilical region that could not be aspirated with wide bore needle. At laparotomy a large bluish opaque sausage shaped appendix was found; it was histologically a mucinous cystadenoma.

Key words:- *Appendix, Mega mucocele, mucinous cystadenoma.*

INTRODUCTION

Mucocele of the appendix is a term used to describe an appendix with a diffuse globular swelling, a dilated lumen with large amount of mucus, and occasional mucinous intraperitoneal collections[1]. Mucoceles of the appendix are rare, appearing in 0.2-0.3 % of surgical specimens[2]. Giant mucocele of the appendix is exceptionally rare as only few cases are reported in the literature over last 10 years. We have used the term Mega instead of giant in our case report. A mucocele of the appendix can be caused by obstruction of the appendiceal lumen, by mucosal hyperplasia, by mucinous cystadenoma or mucinous cystadenocarcinoma[3]. Whatever the cause, obstruction of the lumen and accumulation of yellow mucus within the appendiceal lumen results.

CASE REPORT

A 47 year old male presented with intermittent central abdominal pain for one and a half year and lump in right iliac fossa for one year. Initially he developed intermittent pain in central abdomen, around umbilicus and the area was tender to touch during the episode of pain. The pain was not associated with nausea, vomiting or any other gastrointestinal symptom except that his appetite decreased during the episode of pain. The pain was relieved by taking medicines from a local doctor. He started feeling a small lump in the right iliac fossa, about six months after the start of pain. The lump gradually increased in size and became elongated and tender to touch. He also lost his appetite and developed constipation.

On examination he looked slightly wasted but was not dehydrated or toxic. The abdomen was soft and there was a palpable elongated mass, slightly mobile side to side and tender to touch, in the right side of abdomen. The routine laboratory reports of blood CP, ESR, blood sugar and urea, and urine DR were all within normal limits.

The ultrasound report showed a 102X 42.1-mm size localized collection in right para umbilical region (Fig-1) and advised for aspiration under ultrasound guidance. An attempt for aspiration with wide bore needle under ultrasound guidance was made but nothing could be aspirated.

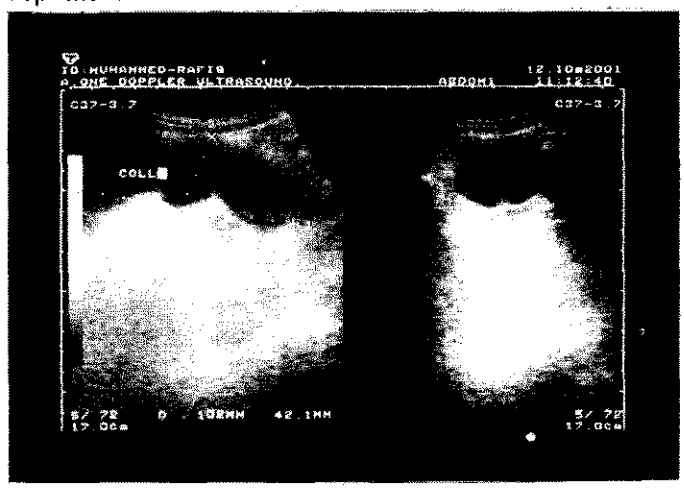

Figure-I: Ultrasound picture showing Mucocele as collection.

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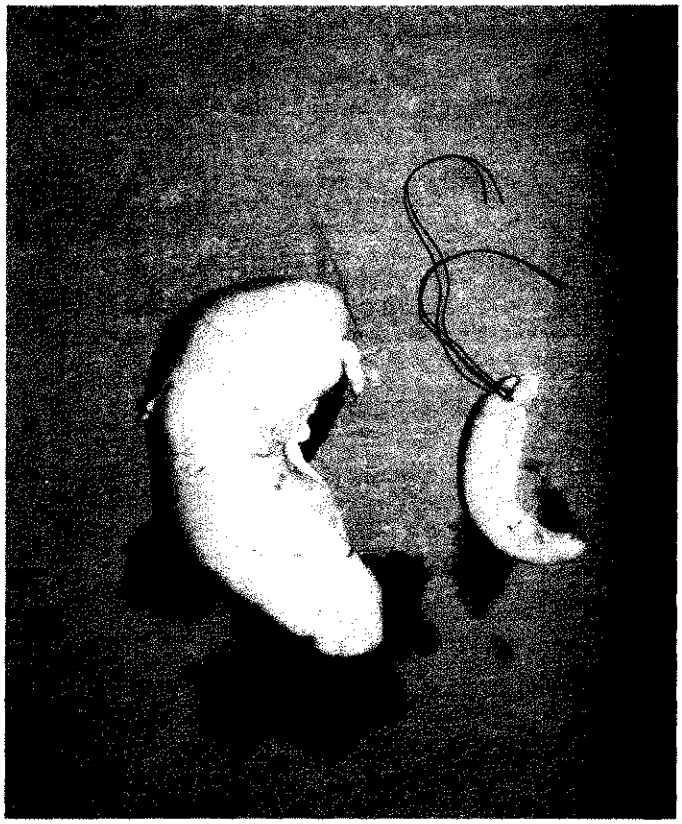

Figure-II: Picture showing the specimen of Mega Mucocele of the appendix compared with the specimen of purulent appendix.

Though clinical findings did not correlate with ultrasound findings, yet a palpable mass looking like a collection on ultrasound that could not be aspirated was mysterious. Hence a decision of an exploratory laparotomy was made. At laparotomy a firm sausage shaped, about 20 X 4 cm bluish opaque mass, easily brought out through the laparotomy wound was seen and it was found to be a very large size appendix (Fig-II). The caecum, colon and all other viscera were normal hence an appendectomy was performed. On gross examination of the appendix, a diagnosis of giant mucocele of the appendix was made. The patient recovered smoothly and was discharged home. He remained well postoperatively. The histology of appendix was mucinous cystadenoma.

DISCUSSION:

Approximately 25% of patients of mega mucocele are asymptomatic. Most present with acute or chronic right lower quadrant pain (64%), but patients have presented with intususception, gastrointestinal bleeding, intermittent colicky pain, abdominal masses, secondary infection and urologic symptoms. Our patient presented with chronic abdominal pain and an abdominal mass.

Investigations like ultrasound [4], CT scan [5] and if possible a barium enema [6] should be performed in order to make a proper diagnosis and exclude other pathologies like fluid filled small bowel, appendiceal / diverticular abscess, appendiceal carcinoid, inverted appendiceal stump, adenocarcinoma of colon etc[7,8]. In our case the ultrasound finding was a collection that could not be aspirated with a wide bore needle. Clinically a mass was palpable on right side of abdomen; hence the decision of exploratory laparotomy was made.

They are pathologically divided into 4 categories [3]. A very rare type is secondary to occlusion of the lumen from post inflammatory scarring, progeric atrophy, congenital obstruction of Gerlach's valve or extramural compression. This type leads to atrophic mucosa. The other types are classified into a spectrum from mucous hyperplasia to mucinous cystadenoma to mucinous cystadenocarcinoma depending on the pathology of the mucosa.

About 25% of mucoceles are from mucosal hyperplasia [9]. These typically have minimal distension. Mucinous cystadenoma, which account for about 60% of mucoceles, are more markedly distended. However, they are typically asymptomatic. Mucoceles up to 40x24x20 cm have been reported[10]. Mucinous cystadenocarcinomas (10-15% of cases) are more likely to be symptomatic, but are extremely rare (benign: malignant about 10:1), and are believed to arise in cystadenomas. There is a high correlation of synchronous or metachronous colorectal adenomas and carcinomas (up to 20% in two series). Thorough investigation of the colorectal tract is recommended after diagnosing an appendiceal mucocecle[11]. Mucinous cystadenomas and cystadenocarcinomas may be indistinguishable grossly but histologically can be differentiated by two features: the first is the invasion of the appendiceal wall by atypical glands; the second is the identification of epithelial cells in any intraperitoneal mucinous collection. The distinction between mucinous cystadenomas and mucinous cystadenocarcinomas is important. Cystadenoma is cured by simple appendectomy, even in the presence of periappendiceal fluid collections, while a right hemicolectomy is the best treatment for a malignant mucinous cystadenocarcinoma in a good risk patient. Rupture of appendiceal mucinous cystadenomas and mucinous cystadenocarcinomas may occur and accounts for about 33 per cent of pseudomyxoma peritonei cases[1]. It is thought by some that pseudomyxoma peritonei is a complication of only mucinous cystadenocarcinoma[12,13]. However, other authors believe this can complicate either benign or malignant mucoceles[4,5], although pseudomyxoma peritonei from the former would carry a better prognosis. Our patient was symptomatic and the size of mucocele was 20X4 cm, and histologically found to be mucinous cystadenoma.

REFERENCES

1. Robb H Rutledge, Primary appendiceal malignancies, Oxford Textbook of Surgery by Peter J Morris and Ronald A Malt 1994; 19.2: 1117-1121.
2. Collin DC. 71,00 human appendix specimens: A final report summarizing forty years study. Am J Proctocol 1963. 14:265.
3. Higa E, Rosai J Pizzimbono C et al. Mucosal hyperplasia, mucinous cystadenoma, and mucinous cystadenocarcinoma of appendix: a revaluation of appendiceal "mucocele".
4. Cancer 1973; 139: 392-400.
5. Skaane, Per, Rudd, Tom E, Haffner, Jon, Ultrasonographic features of Mucocele of the Appendix, J Clin Ultrasound 1988. 16:584-587.
6. Balthazar, Emil J, Computerized Tomography of the Abnormal Appendix, Journal of Computer Assisted Tomography, 1988 12 (4): 595-601.
7. Madwed D, mindelzun R and Jeffrey RB Jr. Mucocele of the Appendix: Imaging Findings. 1992. AJR 159: 69-72.
8. Bahia JO, Wilson MH. Mucocele of the Appendix presenting as an Adenexal mass. J Clin Ultrasound 1989. 17: 62-66.
9. Horgan JG, Chow PP, Richter JO, et al: CT and sonography in the recognition of mucocele of the Appendix. 1984 AJR 143: 959.
10. Mitros, Atlas of GI Pathology.
11. Wallis JW, et al, Giant Mucocele of the Appendix, AJR 1995. 165.
12. Vicenzi L, Moser A, mazzola F, Rizzo S, Bonomo S, Bottura D, et al. Appendiceal Mucocele associated with colonic neoplasm. Report of 2 cases and review of the literature. Chir Ital. 2001. 53 (3): 420-4.
13. Gibbs, NM, Mucinous cystadenoma and cystadenocarcinoma of the vermiform appendix with particular reference to mucocele and pseudomyxoma peritonei. J Clin Pathol 1973; 32: 1525-1541.
14. Dachman A Lichtenstein Friedman A. Mucocele of the appendix and pseudomyxoma peritonei. AJR 1985; 144: 923-929.