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Address of Correspondence
Dr. Mohammad Shakil
Mobile:01612711572, Phone:0818-0121
e-mail: amccjournal@gmail.com

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Editorial

Role of Bisphosphonates in the Treatment of Osteoporosis

Alam MS

Osteoporosis is the most common bone disease. It has been estimated that more than 8.9 million fractures occur annually worldwide and most of these occur in patients with osteopenia or osteoporosis. About one-third of all women and one-fifth of men aged 50 and above suffer fractures at some point in life. [1] Osteoporosis is a disease that is characterized by low bone mass, deterioration of bone tissue and disruption of bone micro-architecture: it can lead to compromised bone strength and an increase in the risk of fractures.[2] Osteoporosis can be classified into two main groups by considering the factors affecting bone metabolism: Primary osteoporosis (Postmenopausal, Senile Osteoporosis) and Secondary osteoporosis.[3] Osteoporosis is easily diagnosed by measuring bone mineral density (BMD) by means of dual X-ray absorptiometry (DXA). As defined by the World Health Organization (WHO) osteoporosis is present when BMD is 2.5 SD or more below the average value for young healthy women (a T-score of <-2.5 SD). A second higher threshold describes "low bone mass" or osteopenia as a T-score that lies between -1 and -2.5 SD. "Severe" or "established" osteoporosis denotes osteoporosis that has been defined in the presence of one or more documented fragility fractures.[4]

Treatment of Osteoporosis include non-pharmacological and pharmacological interventions. A balanced diet should be maintained by all patients diagnosed with osteoporosis. This would include a protein intake of 1–1.5 g/kg/day, adequate intake of calcium and Vitamin-D,lifelong regular weight-bearing and muscle-strengthening exercises, cessation of tobacco use and excess alcohol intake and treatment of risk factors for fall .[5,6]

Most of the current therapies in the prevention of osteoporosis and fractures are designed to decrease bone resorption and they are known as antiresorptive agents. These include estrogen, bisphosphonates (BPs) such as alendronate, risedronate, ibandronate and zoledronic acid; selective estrogen receptor modulators (SERM) raloxifene; human monoclonal antibody against receptor activator of NF-κB ligand (RANKL) denosumab. Bone forming agents (anabolic) are Teriparatide, Abaloparatide (analogs of PTH and PTHrP) and Romosozumab (an injectable monoclonal antibody that inhibits sclerostin) increases new bone formation and decreases bone resorption.[7]

Alendronate at 70 mg/week reduces the risk of fractures (Vertebral: 45%; Non-Vertebral: 25-30%; Hip: 45-55%). Risedronate reduces the risk of all fractures(Vertebral: 39%; Non-Vertebral: 22%; Hip : 27%),it is administered in doses of 35 mg weekly or 75 mg two consecutive days per month.Ibandronate is less effective than other BPs and does not appear to reduce non-vertebral fractures. Zoledronate at 5 mg/year intravenously reduces fractures(Vertebral: 75%; Non-Vertebral: 25%; Hip : 40 %).[8,9]

Adverse effects of oral bisphosphonates on the upper digestive tract are esophagitis and esophageal ulcers. Acute-phase response or flu-like symptoms have been described mainly in response to intravenous BPs. Bisphosphonates treatment (especially intravenous) are associated with atrial fibrillation. Intravenous BPs can result in clinically significant hypocalcaemia (especially when administered to patients with decreased GFRs), risk of developing osteonecrosis of the jaw, incidence of atypical fractures of the femur (AFF). Bisphosphonates are not recommended in patients with renal failure with GFRs ≤30 ml/min.[10,11]

Osteoporosis is a common and silent disease until it is complicated by fractures. DXA scan is the common tool for diagnosis of osteoporosis. Bisphosphonates are the initial pharmacological treatment to reduce the risk of fracture of osteoporotic patients except in renal failure patients. Oral BPs are usually safe and cost effective. Injectable bisphosphonates (Zoledronic Acid) are administered to those who are intolerant to oral BPs. Usually bisphosphonates are given for average 3-5 years to prevent atypical fracture femur. In case of severe osteoporosis anabolic agents maybe given as a first line therapy.

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Dr. Muhammad Shah Alam
Associate Professor, Dept. of Medicine
Army Medical College Cumilla
Email: shahalamdem@gmail.com

Short Term Outcomes of Radial Head Replacement Arthroplasty in Comminuted Radial Head Fracture: Study in a Peripheral Hospital of Bangladesh

Khan MSH[1], Dutta AK[2], Das RK[3]

Abstract

Background: Elbow pain due to radial head fracture is a common presentation to the Emergency Department. Most injuries are isolated, minimally displaced and stable, and require only symptomatic treatment. However, there are unstable variants that must be actively sought and excluded. The radial head is considered the main stabilizer of the elbow when the medial collateral ligament and lateral ulnar collateral ligament have been compromised. The radial head is not only important for humero-radial joint, but also for the stability of distal radio-ulnar joint. In fractures of the radial head, especially complicated with forearm soft tissue injury, proximal migration of radius appears frequently and results in wrist strength weakening and chronic elbow pain. Radial head replacement is indicated for irreparable radial head fractures associated with or without elbow instability. The prosthesis may provide some element of stability, allowing early rehabilitation. This study was aimed to analyze the clinical results after treatment with titanium radial head prostheses, repair of torn soft tissue constraints and early mobilization of the elbow. **Methods:** This is a prospective observational study. From January 2018 to June 2021, 10 patients with radial head fractures were included. Radial Head Replacement (RHR) arthroplasty was performed primarily for irreparable fractures. All patients were followed-up clinically and radiographically for a mean of 20.2 months (range 06 to 36 months). **Results:** On the basis of Mayo Elbow Performance Scores, 7 patients had excellent; 2 good; and 1 fair results. No patient had elbow instability after RHR. Two patients had elbow stiffness 6 months after radial head replacement. None of the prostheses were removed because of loosening or infection. **Conclusion:** Treatment of irreparable radial head fractures with titanium radial head prosthesis and soft-tissue reconstruction at least in the short term, is a safe and effective option for the treatment of severe radial head fractures. Early mobilization of the elbow is important for the restoration of elbow motion and function.

Keywords: Radial head fracture, radial head replacement, post-traumatic unstable elbow.

Introduction

Elbow pain due to radial head fracture is a common presentation to the Emergency Department. It is often caused by an indirect trauma produced by a fall on outstretched hand (FOOSH injury), with the elbow extended and the forearm pronated.[1] Radial head fractures are the most common fractures of the elbow with an estimated incidence of 2.5 to 2.9 per 10,000 people per year[1]. Most injuries are isolated, minimally displaced and stable, and have good functional outcome with conservative treatment. However, there are unstable variants that must be actively sought and excluded.[2] Standard radiographs of the elbow in the antero-posterior and lateral projections should be obtained, as well as a radial head-capitellum view. Displacement and comminution of the fracture are often underestimated on standard radiographs. Computed tomography (CT) provides a more accurate evaluation.[3] Treatment options for radial head fracture include splinting, open reduction and internal fixation (ORIF), early or delayed radial head

1. Lt. Col. Mohammad Shahnewaz Hossain Khan, Classified Orthopaedic Surgeon &Associate professor, Department of orthopaedics and trauma surgery
Army Medical College Cumilla and Combined Military Hospital, Cumilla Cantonment, Bangladesh.
2. Lt. Col. Ashim Kumar Dutta, Classified Specialist in surgery&Associate professor (surgery), Army Medical College Cumilla and Combined Military Hospital, Cumilla Cantonment, Bangladesh
3. Maj. Khaled Hasan, Classified Specialist in surgery& Assistant professor (surgery), Combined Military Hospital, Cumilla Cantonment.
4. Dr. Ripon Kumar Das, Assistant Professor, Dept. of orthopaedics and trauma Surgery, Army Medical College Cumilla

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excision, and radial head replacement (RHR). The optimal management of displaced radial head fractures has not been established. Radial head replacement (RHR) is frequently considered for non reconstructable radial head fractures in the acute setting.[4] The radial head is part of the lateral compartment of the elbow. It articulates with the capitellum to form the humero-radial joint. In addition, the circumference of the radial head articulates with the radial notch of the ulna, forming the proximal radio-ulnar joint. Finally, the radial head is a key component of the forearm scaffold. The blood supply to the radial head is most abundant peripherally, where it derives from metaphyseal arterial branches. These arteries form a terminal network, a configuration associated with a risk of post-traumatic necrosis and non-union.[1] The joint between the radial head and the capitellum is an important stabilizer for axial and valgus loading of the forearm. Approximately 85% of radial head fractures occur in young and active people.[2] According to studies conducted at the Mayo Foundation, the medial collateral ligament is the primary constraint and the radial head is the secondary constraint of the ulnohumeral joint in resisting valgus stress. Biomechanically, the radial head is considered the main stabilizer if the coronoid process is fractured, the medial collateral ligament is incompetent, or the lateral ulnar collateral ligament is disrupted.[5] The critical role played by the radial head in overall stability of the elbow and forearm has motivated many orthopedic surgeons to preserve the radial head during fracture treatment. Excision of radial head only alters kinematics and stability of the elbow. With RHR, the kinematics and stability of the elbow are equal to those of a native radial head.[6] RHR offers better results than radial head excision alone. This study aimed to analyze the clinical results of radial head arthroplasty after treatment of complex elbow injuries with titanium radial head prostheses, along with repair of ligaments where needed to facilitate early mobilization of the elbow.

Material and Methods

Total 10 patients underwent radial head arthroplasty in Moinamoti Cantonment General Hospital between January 2018 and June2021. They were followed up prospectively.The indications for radial head arthroplasty included comminuted and irreparable radial head fracture with or without elbow dislocation, disruption of the medial collateral ligament (MCL), lateral ulnar collateral ligament (LUCL), or forearm interosseous ligament. Information on, age, gender, mechanism of injury and side, and radial head fracture pattern with associated injuries were recorded. All 10 patients had Mason type III fractures of the radial head. Unreconstructable Mason type III fracture of the radial head had prosthesis replacement with a metal radial head implant with or without repair of soft tissue constraints primarily by the same surgeon. Surgical data, including surgical procedures, range of motion (ROM), elbow stiffness, instability before RHR arthroplasty and duration of follow-up were also documented. Table 1 lists the post-RHR range of motion, functional arc, stiffness and instability of the elbow.

Table I: Post radial Head replacement data

SL no	Flexion/ Extension	Supination/ Pronation	Arc of flexion extension	Elbow rotation	Elbow stiffness	Elbow instability
1	120/5	70/65	115	135	nil	nil
2	110/10	70/65	100	135	nil	nil
3	140/0	80/80	140	160	nil	nil
4	125/0	60/65	125	125	nil	nil
5	115/10	80/80	105	160	+	nil
6	135/0	85/85	135	170	nil	nil
7	125/5	85/80	120	165	nil	nil
8	130/5	70/70	125	140	nil	nil
9	120/0	80/80	120	160	nil	nil
10	95/10	70/70	85	140	+	nil

Surgical procedure

All the implants were placed through a lateral Kocher approach, with a skin incision over the lateral or posterior elbow. We choose a lateral skin incision if we did not anticipate repair of the MCL. A posterior approach was preferred for patients with elbow valgus instability. We began a lateral elbow incision superior to the lateral epicondyle and extended it distally approximately 6 cm across the joint in the interval between the extensor carpi ulnaris and the anconeus. We used titanium radial head implants. All the fragments of the radial head were removed, even if radiographic intervention was required. The radial head fragments were recouped to assist in selecting the implant size. A sizing disc was used to select the diameter of the implant. A slightly undersized diameter and thickness were preferred for the prosthesis so the radial head prosthesis articulated congruently with

the capitellum. We resected the remaining radial head at the level of the radial neck fracture, perpendicular to the neck.

Postoperative care

After the procedure, a long-arm splint at 90 degrees of flexion was applied for all patients. Patients with associated ligament injuries, the forearm was splinted for the first 6 weeks. Active flexion and extension exercises were allowed within a "safe" arc of motion as dictated by the associated osseous and soft-tissue injuries. Forearm pronation and supination exercises were advocated actively with the elbow in 90° of flexion or as dictated by the degree of ligament stability. After 6 to 8 weeks, active and passive stretching and strengthening exercises were initiated.

Outcome measures

All patients were followed-up clinically and radiographically for a mean of 20.2 months (range from 6 to 36 months) by the same surgeon. The clinical evaluation was performed using the Mayo Elbow Performance Score (MEPS).[2] The assessment included a record of the patient's pain level, range of movement at the elbow, elbow stability and functional level. Each patient's affected range of movement was compared with the contralateral elbow. The MEPS results were classified as excellent (> 90), good (75–89), fair (60–74), or poor (< 60) (Table 2). Radiographs, including anteroposterior and lateral views of each elbow were evaluated postoperatively at 1 month, 6 months, and 1 year and at the time of final outpatient department follow-up. The radiographs were reviewed for congruity of the radial head with the capitellum, evidence of capitellar osteopenia and erosion, size of prosthesis, periprosthetic loosening, heterotopic ossification, joint incongruity, and osteoarthritis. The size of the prosthesis was evaluated by comparing the widths of the medial and lateral ulnohumeral joint spaces of each patient's operatively treated and uninvolved elbow on follow up anteroposterior radiographs. If the width of the lateral ulnohumeral joint space was increased relative to that in the contralateral elbow or if the medial ulnohumeral joint space was not parallel and was wider laterally (Fig. 3), the prosthesis was considered too thick (overstuffing).[6] We defined radiolucency as any discrete 1-mm region of decreased bone density around the prosthesis. Periprosthetic lucency around the stem was graded as none, mild, moderate, or severe on the basis of the number of involved zones, using a modification of the Gruen classification for the hip,[7] and the amount of lucency was noted in millimeters. Heterotopic ossification was graded with use of the Hastings and Graham classification.[8] The degree of degenerative change was graded with the system outlined by Broberg and Morrey.

Table II: Mayo performance score

Function	Definition	Points	Score classification
Pain	None	45	Excellent >90
	Mild	30	
	Moderate	15	
	Severe	0	
Motion	Arc >100	20	Good 75 - 89
	Arc 50 - 100	15	
	Arc <50	05	
Stability	Stable	10	Fair 60 - 74
	Moderate instability	05	
	Gross instability	00	
Function	Comb hair	05	Poor <60
	Feed	05	
	Hygiene	05	
	Shirt	05	
	Shoe	05	
Total		100	

Results

The outcomes of 10 radial head arthroplasties were reviewed. The patients' median age was 35.25 years (range, 26–63 years). The mean duration of follow-up was 20.2 months (range, 6 - 36 months). Two patients were injured in falls, and the other patient was injured in a motor bike accident. Clinical results Biomechanical study shows that activities of daily living can be accomplished without discomfort within a functional arc of motion of elbow flexion extension of 100°, and forearm rotation of about 100° (pronation 50° to supination 50°)[9]. Therefore we defined elbow stiffness as a functional arc of flexion-extension less than 100° and forearm rotation less than 100°. The range of motion (ROM) of the elbow of the 10 patients after RHR was as follows (Table 3) mean flexion was 121.5° (95° to 140°) mean extension was 4,5° (0° to 10°), mean pronation was

74.0° (65° to 85°) and mean supination was 74.0° (60° to 90°). The mean arc of flexion-extension was 117.0° (85° to 140°) and mean arc of rotation was 149° (125° to 170°). None of the prostheses needed removal because of loosening or infection Radiologic evaluation reveals Implant overstuffing was noted in 3 patients (30%). One patient (10%) patient had radiolucency. There were no instances of capitellar osteopenia, heterotopic ossification, or degenerative changes. Functional results measured by MEPS On the basis of MEPS, 7 patients had excellent results, 1 patient had good results, and the remaining 2 patients had fair results. No patients had elbow instability after RHR. Two patients had elbow stiffness 6 months after RHR (Table 3). No patients had infection or neurovascular injury.

Fig: Radial head arthroplasty
a. Pre- operative X-ray
b. Post- operative X-ray
c & d Per operative X-ray
e & f Follow-up @ 12 months

Table III: Mayo elbow performance score (MEPS) for all patients

No	Pain	ROM	Stability	Function	MEPS
1	30	20	10	20	80
2	45	20	5	25	95
3	45	20	10	25	100
4	45	20	10	25	100
5	15	15	10	20	60
6	45	20	5	25	95
7	45	20	5	20	90
8	15	20	5	25	60
9	45	15	10	25	90
10	45	20	5	25	95

Abbreviation: ROM: range of motion

Discussion

Radial head is not only important for humeroradial joint, but also for the stability of distal ulnoradial joint. In fractures of the radial head, especially complicated with forearm soft tissue injury, proximal migration of radius appears frequently and results in wrist strength weakening and chronic elbow pain.[10] The management of comminuted Mason type III radial head fractures with associated ligament disruption remains controversial. Several surgical options have been advocated for these complex injuries, including ORIF, excision of the radial head, and RHR.[11] The vascular supply to the proximal radial epiphysis is limited to a few small intraarticular vessels coursing along the radial neck and a few intraosseous vessels, resulting in a scanty vascular supply to the radial head. One vessel supplies the radial head directly, entering through the nonarticular anterolateral surface. Consequently, fracture of the radial head is likely to disrupt its vascular supply.[12] In addition, ORIF of a comminuted radial head is often technically difficult. For this reason, in the presence of comminution or severe dislocation of the fracture fragments, as in Mason type III and IV fractures, even a successful osteosynthesis can often result in osteonecrosis of the fragments, pseudoarthrosis, mobilization or failure of the hardware generating a stiff, unstable or painful elbow . In

these cases, the surgical solution involves radial head excision or prosthetization. Simple excision of the radial head in patients with associated interosseous membrane disruption or a medial collateral ligament injury yields poor results, with wrist or elbow instability a frequent outcome. Mikic et al. reported poor results in 50% of patients after excision of the radial head.[13] Josefsson et al. revealed that excision of the radial head may lead to stiffness, weakness and pain. Prosthesis replacement can better restore the stability, flexion and extension of the elbow, and the rotational motion of the forearm. Various prosthetic materials, including silicone rubber, acrylic, cobalt-chromium, vatallium and titanium have been employed. Biomechanical studies have demonstrated that metallic implants restore elbow stability to a level similar to that of the native radial head when a fracture of the radial head occurs in combination with dislocation of the elbow, rupture of the medial collateral ligament, fracture of the proximal ulna, or fracture of the coronoid process.[14] The implant acts as a spacer, allowing soft tissue and ligaments to heal and has enough mobility to adapt to the anatomy of elbow. If the LUCL is intact, prosthetic insertion might be difficult. A retractor should never be placed over the anterior aspect of the proximal end of the radius to avoid injury to the posterior interosseous nerve. If there is coexistent LUCL injury, it may lead to prosthesis overstuffing as result of inserting a prosthesis that is too large. This error should be noted and avoided. There are several issues worth attention in the procedure of prosthetic replacement. There are three critical points during implant of radial head prosthesis: the stability of the stem, the size of the head, the height of the head and the stability of the humero-radial joint.[15] The osteotomy plane of the proximal radius determines whether the prosthesis fits or not. The osteotomised length of the proximal radius must be adjusted accordingly. If it is too short, the implanted prosthesis will be tight. If it is too long, the implanted prosthesis will be unable to make contact with the capitellum and lose its advantage. Several radial prosthesis trial and revision insertions may be necessary to ensure a snug fit. Good axial alignment of the radial prosthetic stem should prevent eccentric rotation of the radius during pronation/supination. The neck of the radius makes an angle of approximately 15° opposing the radial tuberosity with the long axis of the proximal radius. The prosthetic stem should be in accord with the angle. Finally, management of ligament and soft tissue is a critical step, which will determine the results of the surgery. Reconstruction of the annular ligament is a precondition for brachioradial joint stabilisation. We firmly reconstructed the annular ligament with a heavy nonabsorbable suture. Medial and lateral collateral ligament injures and articular capsule injures should be reconstructed whenever possible. Furthermore, early mobilisation for the restoration of elbow function and range of motion are important. In this study, elbow function of the cases fixed with plaster casts was decreased to some extent, whereas the patients who were mobilised early had better recovery. This study was limited by the number of patients included was limited and the duration of follow-up was short

Conclusions Treatment of irreparable radial head fractures with a titanium radial head prosthesis and soft-tissue reconstruction yields satisfactory results. Early mobilization of the elbow is important for the restoration of elbow range of motion and function. Arthroplasty with radial head prosthesis, at least in the short term, is a safe and effective option for the treatment of severe radial head fractures. Studies with a control group and long-term followup are needed for further evaluation.

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Potential Effect of Zinc in Disappearance of Fever in Severe Pneumonia in Children

Ahmed ATMF[1], Hyder RT[2], Sufian A[3],Hossain[4], Majumder RC[5]

Abstract

Background: Zinc deficiency is a global problem affecting populations of low socioeconomic status in both developing and developed countries. It is important micronutrient supporting growth and normal function of the immune system. **Objective:** To observe the effect of zinc causes early disappearance of fever in severe pneumonia in children. **Study Design:** This randomized double blind controlled trial was conducted in the Department of Paediatrics, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from 1st July 2013 to 15th June 2015. **Methodology:** A total 100 patients with severe pneumonia in hospitalized children fulfilling inclusion and exclusion criteria were enrolled by systematic random sampling. Group allocation of Group A and Group B was done by lottery method each consisting 50 and 50 patients. Identical small packet that contained 10mg zinc sulphate powder or 10 mg placebo powder were coded as A and B by guide. **Results:** Temperature was found 101.6±0.5 ^{0}F in placebo group and 101.5±0.5 ^{0}F in zinc group. Temperature did not differ significantly between placebo group and zinc group (p=0.320). Time for normalization of temperature was 34.4±15.2 hours in placebo group and 24.4±4.7 hours in zinc group. Time for normalization of temperature was significantly longer in placebo group than that of zinc group (p=0.001). **Conclusion:** Supplementation of zinc therapy in childhood pneumonia which shows longer time for normalization of temperature in placebo group than that of zinc group.

Key word: Zinc supplementation, fever, childhood pneumonia

Introduction

Childhood pneumonia is common in developing countries, with significant morbidity and mortality. Taking the significance of the problem and variability of risk factors into account, a study was needed to identify the potential determinants of pneumonia in under-five children.[1] Pneumonia accounts for an estimated 1.9 million annual deaths among children under 5 years of age.[2] Zinc deficiency is a global problem affecting populations of low socioeconomic status in both developing and developed countries.[3] Zinc is an important micronutrient supporting growth and normal function of the immune system.[4] Zinc deficiency results in growth impairment, anorexia, behavioural changes, and impaired immune function leading to susceptibility to infections.[5] Studies have shown that in children with pneumonia, the serum zinc level is significantly lower than healthy controls.[6] Prophylactic zinc supplementation can reduce the incidence of pneumonia.[7,8] Zinc regulates various immune functions and protects the health and integrity of the respiratory cells during lung inflammation or injury; thus decreasing susceptibility to acute lower respiratory infections.[9] IAP National Task Force recommended zinc for the treatment of acute diarrhoea.[10] Consensus as to whether zinc

1. Dr. ATM Faruque Ahmed, Associate Professor (CC), Department of Pediatrics, Eastern Medical College & Hospital. Kabila, Cumilla.
E mail- ahmedfaruque8@gmail.com; Mobile: 01812831049
2. Dr. Rumy Tabrez Hyder, Associate Professor of Paediatrics, Jahurul Islam Medical College & Hospital, Bhagolpur, Bajitpur, Kishoregonj.
3. Dr. Abu Sufian, Assistant Professor, Department of Pediatrics, Eastern Medical College & Hospital. Kabila, Cumilla.
4. Dr. Abir Hossain, Assistant Professor, Department of Pediatrics, Eastern Medical College & Hospital. Kabila, Cumilla.
5. Dr. Ripon Chundra Majumder, Assistant Professor, Department of Nephrology, Eastern Medical College & Hospital. Kabila, Cumilla.

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supplementation provides a similar therapeutic benefit to children with severe pneumonia has not yet been established.[11] Many studies were done by different authors on zinc supplementation in severe pneumonia in children but the results of this supplementation on recovery from pneumonia or on the duration of hospital stay were conflicting. Some studies found no role of zinc in clinical recovery and reduction of hospital stay in children with pneumonia.[11,12] While others stated that zinc supplementation enhanced the recovery from severe pneumonia and reduced the duration of hospital stay.[13,14] Zinc-supplementation was given for two weeks only, which may be the reason for no effect of zinc supplementation in prevention of pneumonia episodes in near future.

Materials and methods

A total of 100 patients with severe pneumonia in hospitalized children fulfilling inclusion and exclusion criteria were enrolled by systematic random sampling. Group allocation of group A and group B was done by lottery method each consisting of 50 and 50 patients. Identical small packet that contained 10mg placebo powder or 10 mg zinc sulphate powder were coded as A or B by guide. The patients of group A were treated with coded A packet and those of group B were treated with coded B packet for total of 7 days. Antibiotic and supportive treatment was administered according to WHO guideline. The primary outcome was recovery from severe pneumonia. Fifty patients of Group A and 50 patients of Group B completed the scheduled treatment protocol. Decoding was done by the guide after the completion of the study, coded A blister was placebo and coded B blister was zinc. The patients of group A were treated with code A packet and those of group B were treated with code B packet. Children aged less than 12 months received one packet of code A or one packet of code B, while those aged 12 months or more received two packet of code A or two packet of code B daily for 7 days. Children received code A or code B powder was mixed with breast milk or water and were taken by mouth at the time of enrollment. From day 2, they received one or two packets of their assigned treatment by mouth twice a day for total of 7 days. The standard treatments of severe pneumonia (antibiotic, Oxygen therapy, fluid and nutrition) were given to both groups accordingly.

Results

Table I: Distribution of the patients on baseline characteristics. (n=50)

Baseline characteristics	Placebo group (Group-A) n (%)	Zinc group (Group-B) n (%)
Age (months)		
2-6	12 (24.0)	10 (20.0)
7-24	30 (60.0)	33 (66.0)
25-60	8 (16.0)	7 (14.0)
Mean±SD	11.4±10.5	11.3±9.9
p-value	[a]0.961	
Mean weight (Kg)	7.2±2.7	6.9±2.0
p-value	[a]0.529	
Sex		
Male	38 (76.0)	35 (70.0)
Female	12 (24.0)	15 (30.0)
p-value	[b]0.499[a]	

[a]P value reached from unpaired t-test

[b]P value reached from chi square test

The mean age of placebo group (group A) and zinc group (group B) was 11.4±10.5 months and 11.3±9.9 months respectively. The mean weight was found 7.2±2.7 Kg in placebo group and 6.9±2.0 Kg in zinc group. Thirty eight (76.0%) patients were male in placebo group and 35(70.0%) in zinc group. The difference were not statistically significant (p>0.05) between two groups.

Table II: Temperature in both group before treatment. (n=50)

	Placebo group Mean±SD	Zinc group Mean±SD	p-value
Temperature (^{0}F)	101.6±0.5	101.5±0.5	0.320

[a]P value reached from unpaired t-test

Temperature was found 101.6±0.5 ^{0}F in placebo group and 101.5±0.5 ^{0}F in zinc group. Temperature did not differ significantly between placebo group and zinc group (p=0.320).

Table III: Distribution of the patients by time for normalization of temperature. (n=50)

	Placebo group Mean±SD	Zinc group Mean±SD	p-value
Time to normalization of temperature (hours)	34.4±15.2	24.4±4.7	0.001

P value reached from unpaired t-test

Time for normalization of temperature was 34.4±15.2 hours in placebo group and 24.4±4.7 hours in zinc group. Time for normalization of temperature was significantly longer in placebo group than that of zinc group (p=0.001)

Table IV: Distribution of patients according to adverse effects. (n=50)

Adverse effects (vomiting)	Placebo group	Zinc group
	n (%)	n (%)
Yes	4 (8)	5 (10.0)
No	46 (92.0)	45 (90.0)
p-value	0. 257	

P value reached from chi square test

Adverse effect (vomiting) of treatment was found 4(8.0%) patients in placebo group and 5(10.0%) in zinc group. There was no significant difference of adverse effect of treatment between zinc group and placebo group (p=0.257).

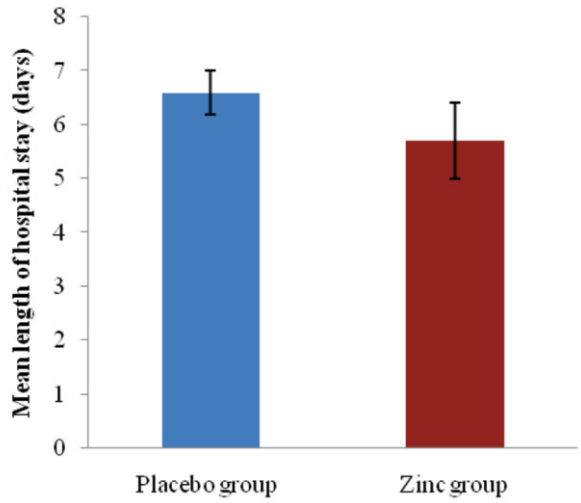

Figure 1: Distribution of patients according to length of hospital stay

P value reached from unpaired t-test

The length of hospital stay was found 6.6±0.4 days (range, 6-7 days) in placebo group and 5.7±0.7 days (range, 5-7 days) in zinc group. Length of hospital stay was significantly longer in placebo group than zinc group (p=0.001).

Discussion

In this study the mean age of placebo group (group-A) and zinc group (group-B) was 11.4±10.5 months and 11.3±9.9 months respectively. The mean weight was found 7.2±2.7 Kg in placebo group and 6.9±2.0 Kg in zinc group. The difference were not statistically significant (p>0.05) between two groups. This result correlated with the study of Basnet et al. where the mean age of the patients in placebo group was 7.1±5.6 months and that of zinc group was 7.8±6.0 months.[15] Sempertegui et al. also found that the mean age of the patients in placebo group was 12.99±11.24 months and that of zinc group was 13.06±10.32 months.[16] In this regards Srinivasan et al. found that mean age was found 17.9±12.2 months in the zinc group and 18.1±11.8 months in placebo group. Shehzadet al. reported that the mean age of participants was 16.65±4.23 months in zinc group and 15.96±5.11 months in placebo group.[14] There was no statistical difference of the age in the two groups. Rerksuppaphol and Rerksuppaphol study observed median age was found 19(10-32) months in zinc group and 17(13-34.5) months in placebo group. The difference was not statistically significant (p>0.05) between two groups.[17] The present study showed thirty eight (76.0%) patients were male in placebo group and 35(70.0%) in zinc group. The difference was not statistically significant (p>0.05) between two groups. This result was supported by Shah et al. in which 43 (67%) patients were male and 21 (32.8%) patients were female in zinc group; while 33 (62.3%) patients were male and 20 (37.7%) patients were female in placebo.[18] The sex of the patients in zinc group and placebo group did not show any statistically significant difference (p=0.578). This result also correlated with the study of Qasemzadehet al. that 35 (58.34%) patients were male and 25 (41.67%) patients were female in zinc group; while 34 (56.67%) patients were male and 26 (43.34%) patients were female in placebo.[19] The sex of the patients in zinc group and placebo group did not show any statistically significant difference (p=0.853). Shehzadet al. reported gender distribution showed 56% (n=84) in zinc group where female and 62% (n=93) in placebo group were males.[14] There was no statistical difference of sex in the two groups. Rerksuppaphol and Rerksuppaphol observed 24 (75.0%) patients were male in zinc group and 19 (59.4%) in placebo group.[17] The difference was not statistically significant (p>0.05) between two groups. In this study

temperature was found 101.6±0.5^{0}F in placebo group and 101.5±0.5^{0}F in zinc group. Temperature did not differ significantly between placebo group and zinc group (p=0.320). Nearly similar findings observed in other studies.[18,20,21] Rerksuppaphol and Rerksuppaphol study observed mean body temperature was found 38.4±0.9 ^{0}C in zinc group and 38.5±0.8 ^{0}C in placebo group.[17] The difference was not statistically significant (p>0.05) between two groups.

In this study time for normalization of temperature was 34.4±15.2 hours in placebo group and 24.4±4.7 hours in zinc group. Time for normalization of temperature was significantly longer in placebo group than that of zinc group (p=0.001). This result correlated with the study of Mahalanbis et al. which found time for normalization of fever was earlier in zinc group.[21] But Srinivasan et al. found that time for normalization of temperature (hours) did not differ significantly between zinc group and placebo group (18.0 and 18.0 hours; p=0.897).[3] Shehzad et al. Comparison of duration of relieve of severe pneumonia signs and symptoms showed 44.62±2.56 hours in zinc group and 48.73±3.124 hours in placebo group with p value of 0.023.[14] Rerksuppaphol and Rerksuppaphol study observed median time to resolution of fever was found 10.0 (4.0-27.0) hours in zinc group and 41.6 (17.0-72.0) hours in placebo group.[17] The difference was statistically significant (p<0.05) between two groups. In this study adverse effect (vomiting) of treatment was found 4 (8.0%) patients in placebo group and 5 (10.0%) in zinc group. There was no significant difference of adverse effect of treatment between zinc group and placebo group (p=0.257). Basnet et al. in their study found that the proportion of children who vomited after the first dose of supplement was higher (14%) in the zinc group than in the placebo group (9%) but did not reach the level of significance (p=0.052).[15] Srinivasan et al. found that two children developed vomiting immediately after receiving the first dose of the intervention: one in the zinc group and one in the placebo group.[3] Subsequent doses were tolerated. Valentiner-Branth et al. found that regurgitation or vomiting within 15 min after supplementation was observed more frequently among children in the zinc group than among those in the placebo group during the supplementation period (37% compared with 13%; odds ratio: 0.25; 95% CI: 0.20, 0.30).[22] In present study the length of hospital stay was found 6.6±0.4 days (range, 6-7 days) in placebo group and 5.7±0.7 days (range, 5-7 days) in zinc group. Length of hospital stay was significantly longer in placebo group than zinc group (p=0.001). Brooks et al. showed shorter durations of hospitalization for the zinc than that of placebo groups.[20] On the other hand, Bose et al. found that there was no significant difference in the median length of hospital stay between the two groups.[11] In the study of Coles et al. the duration of hospitalization was about 20 h longer in the zinc-supplemented group than in the placebo group in suspected bacterial pneumonia (87.3 and 68.3 hours, respectively; HR: 0.56; 95%CI: 0.34, 0.93; P=0.025) and the duration of hospitalization did not differ between the zinc-supplemented group and that of the placebo group in suspected non-bacterial pneumonia (69.5 and 73.2 hours respectively; RR= 1.15; 95%CI: 0.9, 1.50; p= 0.302). Shehzadet al. reported mean duration of hospital stay was 128.31±3.71 hours in zinc group and 137.67±2.56 hours in placebo group (p <0.001).[14] Rerksuppaphol and Rerksuppaphol study observed that mean duration of hospital stay was 3.8±1.3 days in zinc group and 6.1±3.2 days in placebo group.[17] The difference was statistically significant (p<0.05) between two groups.

Conclusion

Supplementation of zinc therapy in childhood pneumonia showed significantly longer time for normalization of temperature in placebo group than that of zinc group.

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Original Articale

A Study on Conservative Management of Chronic Anal Fissure

Hasan K[1], Islam T[2], Quadir E[3], Khan MSH[4]

Abstract

Background: Anal fissure is a common painful condition affecting the anal canal. Majority of acute anal fissure heals spontaneously. However, some of these fissures do not resolve and require some form of definitive treatment. Anal fissure was traditionally treated by anal dilatation or by lateral internal sphincterotomy. Chronic anal fissure is usually associated with internal anal sphincter spasm, the relief of which is central to provide fissure healing. The treatment for chronic anal fissure has undergone a transformation in recent years from surgical to medical. Though surgical treatment has a high success rate, it can permanently impair fecal continence in a large number of patients. A large number of the patients can be cured with the conservative treatment, in addition to the normalization of stools mostly. **Materials and method**: This is a cross-sectional observational study carried out in Colorectal Surgery outpatient department (OPD), CMH, Dhaka from August 2015 to January 2016, a period of six months. Patients diagnosed as chronic anal fissure at colorectal surgery OPD, CMH Dhaka considered as target population and they fulfill the inclusion criteria. All patients were treated with a specific sphincter relaxant 0.2% GTN ointment, stool softener and dietary advice. Though available preparation was 0.4% of GTN, it was diluted with vaseline. **Results**: Total 100 patients were enrolled in this study but 3 cases were dropped out and 1 patient reported good result but failed to attend follow up in hospital but continued treatment as prescribed. The highest incidence was observed in middle age group and most of them belong to the age groups of 25-44 years. Out of 96 cases 56.25% were found male and 43.75% were female There was over all male predominance with a male female ratio 23:18. At the end of 2nd week 66.67% patients had complete symptoms relief, 21.86% patients had partial symptoms relief and symptoms remain unchanged in 11.46% patients. At the end of 8th week 85.42% patients had complete symptoms relief, 4.17% patients were, relieved but recurred and symptoms remain unchanged in 10.42% patients. At the end of 8th week 76.04% patients were highly satisfied, 9.38% patients were moderately satisfied but remaining 14.58% patients were found unsatisfied with treatment. Ulcer at the anus almost completely healed in 85.42% patients, 14.58% patients did not heal upto the mark. Only 27.08% patients developed transient headache among the study group. Beside 12.6% patients developed pruritus ani and 5.21% patients complained of burning in the anal canal after a short period of time after application of GTN ointment. In two patients there was no further improvement of ulcer healing after initial some improvement. **Conclusion**: The present study was designed and attempted to reveal the efficacy of conservative management of chronic anal fissure.. Early diagnosis of these diseases and proper treatment at early stages can save many patients from undue sufferings. The surgical intervention should be done only in patients refractory to appropriate medical treatment. These patients can easily be diagnosed and treated with conservative approach and by appropriate dietary advices.

Keyward: CAF, Conservative management, 0.2% GTN.

Introduction

An anal fissure are longitudinal or eliptical tears or ulcers in the distal anal canal, extending below the dentate line of the anal verge.[1] The fissure is described as acute if it has been present for less than six weeks, or chronic if

1. Major (Dr.) Md Khaled Hasan, Surgical Specialist Combined Military Hospital, Cumilla Cantonment. Mobile: 01769-101492 Email: khaledmihan2@gmail.com

2. Brig. Gen. (Dr.) Md Tanvirul Islam, Fellow Colorectal Surgery (NUH Singapore)
Adviser Colorectal Surgery, Combined Military Hospital, Dhaka. Dhaka Cantonment.

3. Col. (Dr.) Md Ershad-Ul-Quadir, Classified Surgical Spl, Combined Military Hospital, Cumilla Cantonment.

4. Lt. Col. (Dr.) Md Shahnewaz Hossain Khan, Classified Orthopedic Surgeon, Combined Military Hospital, Cumilla Cantonment.

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present more than six weeks or recurrent fissures, are generally defined as chronic. Chronic anal fissures have distinct anatomical features such as visible sphincter fibers at the fissure base, anal papillae, sentinel piles and indurated margins.[2] Once a fissure develops, the internal anal sphincter typically goes into spasm, causing further separation of the tear impairing healing and causing pain. Exposure to feces also slows healing.[3] Anal fissures are usually caused by trauma that stretches the anal canal, such as after passage of large or hard bowel movement or explosive diarrhoea. Less commonly, fissures are caused by foreign body insertion or anal intercourse.[3,4] Anal fissures can also occur in patients who have other medical conditions such as Crohn's disease. Patients with an anal fissure may first note bleeding and a sensation of tearing, ripping or burning following a bowel movement. Once a fissure develops, these symptoms can occur after every bowel movement; the rectal pain can last several minutes to hours. Bleeding is usually mild and limited to a small amount on toilet paper or the surface of stool. Atypical features such as multiple, large, or irregular fissures, or those not in the midline, may indicate underlying malignancy, sexually transmitted infections, inflammatory bowel disease or trauma. Anal fissures can usually be diagnosed based on the symptoms described above and a physical examination. A careful history usually suggests that an anal fissure is present and gentle inspection of the anus can confirm the presence of a fissure. The physical examination involves gently separating the buttocks, allowing for visual inspection of the region around the anus. A fissure most commonly appears in the 12 or 6 o'clock position. Chronic anal fissures typically occur in the midline with visible sphincter fibers at the fissure base, anal papillae, sentinel piles, and indurate margins. A rectal examination or endoscopy can often be avoided in the initial diagnosis of a fissure. Once healing has occurred or if the diagnosis is unclear, a sigmoidoscopy or colonoscopy is usually recommended, especially if there has been rectal bleeding. The goal of treatment for anal fissures is to relieve the pain and spasm and heal the fissure. Initial treatment is aimed at eliminating constipation, softening stools and reducing anal sphincter spasm.

Materials and Methods

A cross-sectional observational prospective study was carried out in colorectal surgery outpatient department of CMH Dhaka from August 2015 to January 2016 a period of six months with clinical features of chronic anal fissure. Inclusion criteria was those patients attended at surgery OPD, CMH Dhaka diagnosed as chronic anal fissure and Age > 15 years, exclusion criteria was anal fissure associated with other diseases like tuberculosis, inflammatory bowel disease, malignancy, anal fissure associated with 2° or 3° haemorrhoid, age < 15 years, pregnant patient, patient with IHD.

Results

Table I: Age incidence (n=96)

Age group (years)	No. of patients	Percentage(%)
15-24	13	13.54
25-34	37	38.54
35-44	29	30.21
45-54	14	14.58
>55	03	03.13

Table II: Sex distribution (n=96)

Sex	No. of patients	Percentage(%)
Male	54	56.25
Female	42	43.75

Table III: Symptoms relief at the end of 2nd week (n=96)

Symptoms	No. of patients	Percentage(%)
Complete relief	64	66.67
Partial relief	21	21.86
Unchanged	11	11.46

Table IV: Symptoms relief at the end of 8 week (n=96)

Symptoms	No. of patients	Percentage (%)
Complete relief	82	85.42
Relieved but recurred	04	4.17
Unchanged	10	10.42

Table V: Patient's satisfaction with the outcome of the procedure (n=96)

Symptoms	No. of patients	Percentage (%)
Highly satisfied	73	76.04
Moderate satisfied	09	9.38
Not satisfied	14	14.58

Table VI: Rate of ulcer healing (n=96)

Ulcer healing	No. of patients	Percentage (%)
Healed	82	85.42
Not healed	14	14.58

Table VII: List of complications (n=96)

Name of complications	No.of patients	Percentage (%)
Headache	26	27.08
Pruritus	12	12.50
Transient burning in anal canal	5	5.21
Tolerance	2	2.08

Out of 96 patients who were enrolled in this study 54 (56.25%) cases were male and 42 (43.75%) were female. Total hundred patients were enrolled in this study but 3 cases were dropped out and one patient reported good result but failed to attend follow up hospital but continue treatment as prescribed. At the end of 2nd week 64 (66.67%) patients had complete symptoms relief 21 (21.86%) patients had partial symptoms relief and symptoms remain unchanged in 11(11.46%) patients (Table 3). At the end of 8th week 82 (85.42%) patient had complete symptoms relief, in 4(4.17%) patients symptoms were relieved but recurred and symptoms remain unchanged in 10 (10.42%) patients.(Table-4)

At the end of 8th week 73 (76.04%) patients were highly satisfied, 09 (9.38%) patients were moderately satisfied but remaining 14 (14.58%) patients were unsatisfied with treatment. Ulcer at the anus almost completely healed in 82 (85.42%) patients out of 96 patients. Ulcer healing in rest of 14 (14.58%) patients was not up to the mark. The age of the patients >15 years were include in this study. The highest incidence was observed in middle age group and most 66 (68.75%) of them belongs to the age groups of 25-44 years. Mean age was 35 years and incidence was lowest in elderly. Only 26 (27.08%) patients developed transient headache. Beside these 12(12.50%) patients developed pruritus and 5(5.21%) patients complained of burning in the anal canal for a short period after application of GTN. (Table-7) In two patients there were no further improvement of ulcer healing and symptoms relief after initial some improvement and were prescribed of 0.4% GTN ointment, in increase concentration of GTN there were complete ulcer healing.

Discussion

Chronic anal fissure is a common condition. The pathophysiology of chronic anal fissure is still not clear. Ischaemia with hypertonia of the internal anal sphincter probably the main cause of development of anal fissure. Although typical fissure are commonly described as idiopathic, current evidence suggests they are caused by high sphincteric pressure and secondary to local ischaemia.[5] Operative treatment decreases sphincter pressure either by forceful dilatation or now far more commonly, by lateral internal sphincterotomy. Although this technique is a sample and effective outpatient surgical procedure performed under local anaesthesia, its fundamental drawback is its potential to cause minor but sometimes permanent alterations in the control of gas, mucous and occasionally stool.[6,7] Surgical procedures may cause impairment of continence in up to 30% of cases.[8] There complications have led to a search for alternative therapies for the treatment of chronic anal fissure.[9] In this study total 96 patients were enrolled but 96 patients complied the protocol. The age of the patients more than 15 years were included in this study and highest incidence was observed in middle age group and most 66 (68.75%) of them belong to the age group of 25-44 years. Mean age was 35 years (range 15 to 65 years) which shows small variation with the study of Moosavi SR et al (2007)[10], the mean age was 34 years, ranging from 24-52 years and Oh C et al (1995)[4] found that average age was 39 years. This variation may be due to variation in age range of different study. Out of 96 cases 54 were male 42 were female. Male female ratio 54:42=1.77. This data did not approximately correlate with others study. The studies of Mazieret et al.[12] showed that male female ratio is equal. This variation is due to our social environment where less number of female patients attend in outpatient department and also may be for aversion to expose to male surgeon. Out of 96 patients, symptoms relieved at the end of 8th week completely in 82 (85.42%), in 4 patients (4.17%) symptoms relieved but recurred and unchanged in 10 (10.42%) cases. Ulcer healing occurred in 82 (85.42%) cases and shows 0.2% GTN causes significant ulcer healing in case of anal fissure.In case of patients satisfaction with the outcome of the procedure 73(76.04%) were highly satisfied and 9(9.38%) case were moderately satisfied. The data correlate with the other studies. Ward DL et al.[13] found in their study that 12 of the 16 patients (75%) were cured. Of these, symptomatic relief was obtained for most within 2 days and for all within one week. In present study 64 out

of 96 patients 66.67% had complete relief of symptoms at the end of second weeks. Palazzo E F et al. shows in their study that 33 of 45 patients (75%) had clinically healed ulcer with the 0.1% GTN paste over all at 12 weeks following treatment.[14] But in present study with the use of 0.2% GTN ointment 82 (85.42%) of 96 patients were cured within 8 weeks. Chaudhuri S, et al. showed in their study fissure healed in 7 of 10 patients treated with GTN and 2 of 9 patients treated with placebo.[15] In their study they found 70% cases were clinically healed with treatment. In a randomized study Oettle G J, et al. found 10 of the 12 (83.3%) healed with local glycerinetrinitrate and concluded, local application of glycerinetrinitrate can avoid surgery in more than 80% patients with chronic anal fissure.[16] This result is closely consistent with the present (85.4% cases completely healed) study. Local application of exogenous NO donor such as nitroglycerin and isosorbiddinitrate reduces anal pressure and improves anodermal blood flow. This dual effect reduce fissure in more than 80% of patients, is also consistent with present study.[17] Tander B et al. showed that in children GTN was superior to placebo, with relief of symptoms in over 90% of GTN treated patients.[18] In my study, age group started from >15 years, children were not included. Lund JN and Scholefield JH showed in their study that topical GTN provides rapid, sustained relief of pain in patients with anal fissure. Over two third of patients treated in this way avoid surgery which would otherwise have been required for healing. Complication of the procedure such as headache, burning in the anal canal, pruritus occurred. Among the study population 26 (27.08%) patients complaint of headache, pruritus in 12 (12.50%) patients, burning sensation in anus in 5 (5.21%) of cases. In other studies the incidence of headache appeared much higher in comparison to present study. The low incidence in our patient population is due to poor socioeconomic condition, where they are reluctant to report to physician with this minor symptom. The reports of complication are variable in different studies. In this study none discontinued treatment for complications and all complications were mild to moderate in nature and transient. Although 58% of the patients treated with GTN experiences headache at some point during treatment only one patient stopped treatment due to this side effect. Many patients affected by headache observed that the headache was far less painful than pain previously experienced on defecation.[19] Scholefield et al showed that the severity of headache with topical GTN therapy is dose dependent and formulation containing 0.1% GTN could be effectively used in chronic anal fissure.[20] Gorfine reported that 30% of the patient experienced transient headache when treated with topical 0.3% nitroglycerine ointment but that all are able to continue treatment.[21]

Conclusion

Anal fissure is a common condition affecting all age groups, but it is seen particularly in young and otherwise healthy adults, with equal incidence across the sexes. The aim of this trial was to explore the efficacy of conservative treatments with 0.2 percent gjyceryl trinitrate and some form of general measures in the treatment of chronic anal fissure in terms of fissure healing, pain relief, relief from bleeding during defecation, itching and pruritus. Complication of treatment like headache was managed easily and incontinence for feces and flatus do not develop. It shows that up to 85.4% of patients with chronic anal fissures can be successfully treated using topical 0.2% GTN paste as a primary measure. Lateral sphincterotomy remains effective option but should be reserved for patients who fail to respond to initial conservative management. Present study concluded that local application of GTN, laxative and changing in dietary habit could avoid surgery in more than 80% of patients with chronic anal fissure.

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Original Articale

Diagnostic Laparoscopy to Delineate the Diagnostic Dilemma of Chronic Abdominal Pain

Dutta A K[1], Quadir E U[2], Khan S H[3], Johny M A[4]

Abstract

Introduction: Chronic abdominal pain is a very common problem for both the medical and surgical care professionals. These patients are usually evaluated by different types of diagnostic investigations but no definite cause of their problem could be detected. Diagnostic laparoscopy visualizing the entire peritoneal cavity, allows us to take biopsies if needed. Laparoscopy also useful as a therapeutic tool for many cause of chronic abdominal pain. **Methods**: Our study included 50 patients with a history of chronic abdominal pain of 4 months or more duration from January 2018 to December 2020 in Combined Military Hospital, Jashore with unremarkable clinical examination, base line investigations and imaging studies. Outcome measured included the overall efficacy of diagnostic laparoscopy to diagnose the cause of chronic abdominal pain and response to pain after 4 months of procedure. **Results:** In this study, we select 47 patients where 36 were female and 11 were male with an average age of 35 years who underwent diagnostic laparoscopy for the evaluation and treatment of chronic abdominal pain. The average duration of pain was 8 months. We achieved definitive diagnosis in 47(94%) patients by diagnostic laparoscopy. It helps in initiation of appropriate treatment in this difficult patients group. Pain response in the form of positive outcome (relieved / reduction) was seen in 44 (93.62%) patients. **Conclusion:** Diagnostic laparoscopy is a simple, rapid, relatively cost effective and efficient method of establishing the accurate diagnosis in patients with chronic abdominal pain with the advantage that it is an effective therapeutic tool.

Key wards: Chronic abdominal pain, Diagnostic laparoscopy, Pain relief after specific management.

Introduction

Surgical and medical care professionals often remain in emergency with the issue of chronic abdominal pain in patients. Chronic abdominal pain is one of the common clinical presentations in general surgical practices.[1] Commonly, such patients suffers for long duration and are subjected to ample of diagnostic investigations suggested by the physician without revealing a specific etiology due to various dilemma.[2] Surprisingly, more than 40% of chronic abdominal pain patients without definitive diagnosis are treated as functional condition such as, Functional Dyspepsia, Irritable Bowel Syndrome and Motility Disorders.[3,4] Several other organic conditions may be responsible for the chronic abdominal pain in patients which include Appendicular causes, Intestinal Adhesions or some other rare or little known conditions.[5] Failure of multiple investigation efforts to understand the reason of the pain leads to referring the case to the consultation of surgeons with an assumption that surgical intervention may provide insight into the cause of the pain and lead a path to remedy. Considering such situations, appendectomy and laparotomy used to be recommended previously.[6] Laparoscopy is as much a surgical procedure as exploratory laparotomy and very often, just as informative. With the introduction of laparoscopic surgery, a new tool has been added to our knowledge. The use of this new technology in the diagnosis and

Correspondence: Lt Col Ashim Kumar Dutta, Classified Specialist in Surgery, CMH Cumilla, Cumilla Cantonment. Cell No: 01712248899. Email: asimdr29@gmail.com

1. Lt Col Ashim Kumar Dutta, Classified Specialist in Surgery, CMH Cumilla.
2. Col Md Ershad Ul Quadir, Classified Spl in Surgery, CMH Cumilla.
3. Lt. Col. Md Shahnewaz Hossain Khan, Classified Spl in Orthopedics, CMH Cumilla.
4. Dr. Md Mahbubul Alam Johny, Assistant Registrar, Department of Surgery, Army Medical College, Cumilla.

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management of chronic abdominal pain has been tried earlier by the various author.[7,8] Laparoscopy can identify abnormal findings and improve the outcome in a majority of patients with chronic abdominal pain, as it allows surgeons to see and treat many abdominal conditions that cannot be diagnosed otherwise.[9,10] Apart from visualizing a large part of the abdominal cavity, a precise targeted biopsy, fine-needle aspiration cytology or fluid analysis can also be done. In case of diagnostic uncertainty, laparoscopy may help to avoid unnecessary laparotomy, provides accurate diagnosis, helps to plan surgical treatment, improves the outcome in the majority of patients with chronic abdominal pain and allows surgeons to diagnose and treat many abdominal conditions that cannot be properly managed otherwise.[11] It is a safe and effective tool, which can establish the cause and allows for appropriate interventions in such cases[12] The purpose of this study was to assess the benefit of performing diagnostic and therapeutic laparoscopy in patients with chronic abdominal pain.

Material and Methods

This study is a expected clinical trial, which was established in CMH, Jashore included50 (39 female and 11 male) consecutive patients over a period of 3years (January 2018 to December 2020) presenting with a history of chronic abdominal pain for more than 4 months with unremarkable clinical examination. Demographic data of patient were listed in Table 1 with Pie chart. After detailed history from patients and thorough clinical examination, the findings were recorded in the proforma. Basic investigations were done for the patient. Based on the clinical examinations and imaging studies patients were subjected to diagnostic laparoscopy and the necessary surgical methods were employed as per the etiology after taking informed valid written consent. This study also included patients who were admitted to the hospital with a history of chronic abdominal pain for more than 4 months duration with the unremarkable clinical examination, laboratory and imaging studies, and underwent diagnostic laparoscopy. Patients were followed up at regular intervals after 7 days of post-discharge and then 4 months after the procedure. Subjective assessment of pain was done by asking the patients, what occurred to their pain: relief, reduced or no change. The findings and outcomes of laparoscopy were recorded and analyzed. Outcome measured included the overall efficacy of diagnostic laparoscopy in finding a cause of chronic abdominal pain, diagnosis made, post-operative complications, response to pain after 4 months of procedure. Ethical consideration: Approval was obtained from the institutional ethical committee. All data were analyzed using the SPSS.

Results

In this study, patients age range is in between 20 to 50 years (mean 35years) and total patient is 47 (male 11 and female 36). In our study, it was able to achieve definitive diagnosis in 47 patients. After every diagnostic laparoscopy every patient should be assessed, consulted and advised for regular follow up in OPD of Surgery department of CMH, Jashore. It led to initiation of appropriate treatment in this difficult patient group and pain response in terms of positive outcome (relief/ reduction of pain after diagnostic laparoscopy) was seen in 44 (93.62%) of the patients. The analysis of pain response in patients shows that the association between age group and pain response is not statistically significant. Our study also showed that chronic abdominal pain is a common problem among the female population with incidence being 78%. Patients presented with varied duration of pain ranging from minimum of 4 months to maximum12 months with mean duration of pain being 8months. After clinical evaluation the most common location of pain is in the abdomen. In our study was right lower quadrant seen in 18 patients (38.30%) followed by diffuse pain in 13 patients (27.66%). The most frequent operative findings were adhesions noted in 53.19% of the patients in our study. (Table 1). The history of previous abdominal surgery was present in 31 patients (65.96%) and surprisingly in 21 out of 31 patients, i.e., (67.74%) adhesions were found. It was observed in our study that most patients with abdominal pain with intra-abdominal adhesions respond well to laparoscopic adhesiolysis. Thus, the most common diagnosis in our study was post operative band and adhesions 21 patients (44.68%). This is most common cause of the chronic abdominal pain was Abdominal Tuberculosis diagnosed in 10 (21.28%) patients. In our study, 47(94%) patients had pathological findings identified at the time of laparoscopy and therapeutic interventions were carried out based on the findings obtained on diagnostic laparoscopy to achieve a cure. Various therapeutic interventions that were carried out to achieve cure included Adhesiolysis (53.19%), Appendectomy

(17.02%), Cholecystectomy (2.13%), Cyst aspiration (2.13%), Laparoscopic inguinal hernioplasty (2.13%). Thus, in overall 72% patients, therapeutic interventions were carried out in our study. Therapeutic interventions were carried out in 37 patients (78.72%) out of 47 and 35 patients (94.59%) gave history of positive response. At the time of follow-up after 4 months (Table 2). Relief of pain was noted in 40 patients (85.11%), 4 patients (8.51%) had reduced pain with 3 patients (6.38%) having persistent pain after diagnostic laparoscopy with overall positive response to pain in 44 (93.62%) of patients in our study. In our study, 03 patients had a negative diagnostic laparoscopy and free fluid was found in pelvis of 01 patient, which was aspirated and sent for analysis. However, the fluid analysis was normal and hence in all 04 patients (8.51%) were observed to have no cause or pathology attribute able to their chronic abdominal pain, and they were labeled as Idiopathic chronic abdominal pain. However, 03 out of these 04 patients (75%) responded positively after diagnostic laparoscopy.

Table I: Showing distribution of operative findings on diagnostic laparoscopy (n= 47)

Operative findings	No. of patients	Percentage (%)
a) Adhesions		
1. Post-op adhesions	21	44.68
2. Adhesions due to congenital bands	3	6.38
3. Inflammatory adhesions	1	2.13
b) Abdominal tuberculosis	10	21.28
c) Inflamed appendix	8	17.02
d) Left indirect inguinal hernia	1	2.13
e) Right ovarian cyst	1	2.13
f) Thickened gall bladder wall+dense adhesions	1	2.13
g) Free Fluid	1	2.13

Table II: Showing final diagnosis, management and positive outcome (n=47)

Diagnosis	Management	No. of patients n (%)	Positive outcomen (%)
Bands and Adhesions	Adhesiolysis	25 (53.19)	24 (96.00)
Abdominal tuberculosis	ATT	10 (21.28)	9 (90)
Recurrent appendicitis	Appendectomy	8 (17.02)	7 (87.5)
Left indirect inguinal hernia	Laparoscopic inguinal hernioplasty	1 (2.13)	1 (100.0)
Right ovarian cyst	Cyst aspiration	1 (2.13)	1 (100.0)
Acalculouscholecystitis	Cholecystectomy	1 (2.13)	1 (100.0)

Table III: Showing pain response in follow up patient who are managed after diagnostic laparoscopy

Pain response (follow-up after 3 months)	No. of patients	Percentage(%)
Relief	40	85.11
Reduced	4	8.51
Persistent	3	6.38

Discussion

Diagnostic laparoscopy is now a day a well-accepted diagnostic technique throughout the world. Recent advances in this technology and increasing expertise in laparoscopy has established the safety of this procedure with certainty.[13] Diagnostic laparoscopy allows the surgeon to see surface anatomy of intra-abdominal organs with greater details better than any other imaging modality. However, laparoscopy has got its own limitations such as non-visualization of deep parenchymal organs, processes of retroperitoneal space and the inner surface of hollow organs, and not allowing the surgeon to palpate the organs.[14] Idiopathic chronic abdominal pains are among the most challenging and demanding conditions to treat across the whole age spectrum. Potentially it can be unrewarding for both patients and the medical team. Abdominal pain was the third most common problem of individuals enrolled in a large health maintenance organization.[15] All patients included in this study had chronic abdominal pain, they were subjected to laparoscopic evaluation after exclusion of all organic causes of the pain by detailed history, complete clinical examination, laboratory tests, radiographic evaluations, and upper gastrointestinal or lower gastrointestinal endoscopy were applicable. In our study we find definitive pathological finding in 47 out of 50 patients which is 94.00% and we started definitive management. So it confirmed that in this difficult patient group, laparoscopy could safely identify abnormal findings and can improve the outcome in a majority of cases. In this study, 47 (94%) patients had pathological

findings identified at the time of laparoscopy. This percentage is almost similar when compared with other studies such as Karl miller et al.[16] who reported that laparoscopy provided diagnoses in 89.8% of patients. In this study, the most common finding was post-operative band & adhesions in 25 (53.19%) patients and the second common cause of chronic abdominal pain was abdominal tuberculosis in 10 (21.28%) patients and the third common cause was chronic appendicitis in 8 (17.02%) patients. Our findings was almost similar the result published by Koltset al.[17] In our study 03 patients did not have any pathological findings on laparoscopy. Two of these patients had resolution of pain after diagnostic laparoscopy. Our findings was almost similar the result published by Hussain et al.[28] This study proves beyond doubts that diagnostic laparoscopy can be considered as an option in patients with chronic abdominal pain. The overall positive outcome seen in the above mentioned studies after diagnostic laparoscopy compare favorably with the results obtained by us. Hence, it can be concluded that it has an effective diagnostic role in evaluating patients with chronic abdominal pain, in whom conventional methods of investigations have failed to elicit a certain cause. The therapeutic value of diagnostic laparoscopy is also accepted, well-appreciated. Being minimally invasive, laparoscopy has solved the problem of delay in the definite diagnosis and has led to considerable reduction in the number of negative exploratory laparotomies. It has also significantly reduced the number of investigation these patients are subjected to, days of hospital stay, which leads to substantial reduction in the cost of the treatment.

Conclusion

Diagnostic laparoscopy is able to achieve the final diagnosis and provide tissue diagnosis without any significant complication and less operative time. The therapeutic value of diagnostic laparoscopy is accepted and well appreciated. So it can be safely concluded that diagnostic laparoscopy is a simple, rapid, effective and accurate tool in evaluating patients with chronic abdominal pain for establishing a conclusive diagnosis. Diagnostic laparoscopy also solves the problems of dissatisfaction of both the surgeon and the patient, which is one of the important issues in the treatment of these difficult patient groups.

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Original Articale

Comparison between Midazolam and Clonazepam as Premedicant to Reduce Anxiety in Patients Undergoing Elective Surgery under General Anaesthesia

Karim ME[1], Chowdhury AI[2], Ershad R[3]

Abstract

Background: The majority of patients admitted to hospital for elective surgery experience anxiety preoperatively which can adversely influence the surgical procedure as well as the patient's recovery. Reduction of anxiety and fear at preoperative period in patients of elective surgery is essential for surgical preparation. Benzodiazepines are the most commonly used drugs for this purpose. This study compares the anxiolytic effects of Midazolam and Clonazepam before surgery under General Anaesthesia. **Materials and Methods:** This randomized clinical trial was carried out in series of 60 consecutive, randomly selected patients, aged 18-60 years, admitted for the elective surgery under General Anaesthesia, in Combined Military Hospital, Chattogram during the period of September 2019 to February 2020. Patients receiving Midazolam or Clonazepam as preoperative medication were included in the study. Anxiety was scored using VAS (Visual Analogue Scale), sedation was scored by using Ramsay Sedation Scale and anterograde amnesia by asking preoperative events after 24 hours of premedication. **Results:** Mean anxiety reduction was significantly more in Clonazepam group compared to Midazolam group (P value 0.04 vs 0.48). Sedation level was less with Midazolam compared to Clonazepam (mean 1.56 vs 2.36, P<0.05). Significant percentage of patients could not recall preoperative events in Clonazepam group compared to Midazolam group (average 67.77% vs 27.77%, P<0.05). Overall incidence of adverse effects was significantly more in Midazolam group compared to Clonazepam group (23.33% vs 3.30%, P<0.001). **Conclusion:** The standard administration of Clonazepam before procedure provides patients with a moderate reduction of periprocedural anxiety. Premedication of Midazolam is associated with a high incidence of adverse effects. Therefore, this study favors routine use of Clonazepam as premedication to reduce anxiety before surgery.

Keywords: Midazolam, Clonazepam, Premedication, Anxiety.

Introduction

Many patients develop negative emotions when they are scheduled for a surgical procedure. These may include anxiety, depression, aggression, fatigue and physical complaints. Anxiety is the most well known and prominent preoperative complaint. Preoperative anxiety can have adverse effects on the perioperative course because it correlates with high postoperative anxiety, increased postoperative pain, increased need for analgesics, postoperative nausea and vomiting and prolonged hospital stay. Furthermore it has been shown that preoperative anxiety has a negative effect on the induction of anaesthesia and recovery.[1-3] Drugs of different classes like sedative-anxiolytic drugs, opioids, anticholinergics, neuroleptics, H2 blocker and antiemetics have been used for premedication. The purposes of preoperative medication are to prevent psychic shock, to regulate metabolism, elimination of any stage of excitement, and the possibility of maintaining a lighter degree of anaesthesia or of using a less toxic anaesthetic that would otherwise be required.[4] Preoperative treatments also aim at reducing the emergence agitation occurring during recovery.[5-7] Incidence of anxiety has been found variable in different

1. Colonel Md Enayet Karim, Classified Specialist in Anaesthesiology, Combined Military Hospital, Chattogram.

2. Major Arif Imtiaz Chowdhury, Graded Specialist in Anaesthesiology, Combined Military Hospital, Chattogram.

3. Brig Gen (Retd) Reza Ershad, Professor of Anaesthesiology, East West Medical College and Hospital, Dhaka.

Correspondence: Colonel Md Enayet Karim, Email: enayet852@yahoo.com, Mobile: 01739988644

studies. Overall rate of anxiety was observed in 72.7% patients scheduled for elective caesarian section. Around 23.4% patients were found to be anxious regarding General Anaesthesia (GA). Female showed a higher incidence of anxiety (35.1%) than male (11.1%). The incidence is high in those having lower educational level. Human emotions like acute emotional arousal increases sympathetic activity.[8,9] Anxiolytic premedication by benzodiazepines could be a useful treatment for patients who suffer from preoperative anxiety. Benzodiazepines increase the effect of the natural neurotransmitter gamma-aminobutyric acid at the receptor site in the brain, which initiates a reduction of neuron excitability with consequently anxiolytic, sedative and amnesic effect. The effectiveness of anxiolytic premedication critically depends on the anaesthesiologist's ability to detect anxiety during the preoperative visit.[10-12] This evaluation provides the frequency of the use of Midazolam or Clonazepam as preoperative medication in the elective surgeries. This study has been undertaken with a view to evaluate the comparative efficacy of Midazolam and Clonazepam regarding onset, duration and degree of anti anxiety, sedation and amnesia during surgery under general anaesthesia.

Methods

The study was carried out in series of 60 consecutive, non selected patients, aged 18-60 years, admitted for the elective surgery under General Anaesthesia after obtaining written consent, in Combined Military Hospital, Chattogram during the period September 2019 to February 2020. Patients receiving midazolam and clonazepam as preoperative medication were taken. Patient of either sex, different ages with mild to moderate systemic disease (ASA I and ASA II) and all the patients for elective surgery under GA were taken as subjects. Exclusion criteria were pregnant or lactating female, patients with decompensated hepatic or renal disease, those unwilling to give informed consent, hypersensitive to or had contraindications to the use of benzodiazepines or use of any CNS depressant for any reason, history of alcohol, benzodiazepines or other drug abuse.

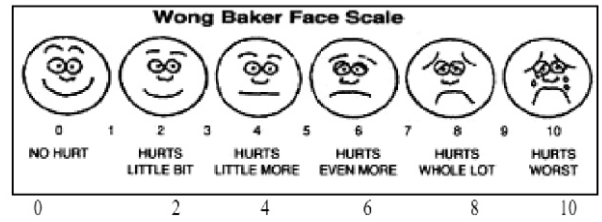
Thirty patients were premedicated with midazom (7.5mg) orally two hours before surgery and 30 patients were premedicated with clonazepam 1mg orally. The assessment of anxiety and vital signs were done immediately before drug administration. The efficacy assessment like anxiety and sedation were done after drug administration before taking the patient in Operating Room (OR). However, the anterograde amnesia was assessed after 24 hours of premedication.

Anxiety was scored using VAS (Visual Analogue Scale), sedation was scored by using Ramsay Sedation Scale and anterograde amnesia by asking preoperative events after 24 hours.

Ramsay Sedation Scale:

Sedation level	Description
1	Anxious and agitated
2	Cooperative, tranquil, oriented
3	Responds only to verbal commands
4	Asleep with brisk response to light stimulation
5	Asleep without response to light stimulation
6	Non responsive

Visual Analogue Scale:



Anterograde Amnesia:

Being taken into the operation: A

Being shown the surgical light: B

Being shifted from stretcher to the operating table: C

Data was recorded on predesigned proforma and statistical analysis (student's 't' test) was done to carry out the output. Data were expressed in mean, SD and percentage. The value $p<0.05$ was considered statistically significant. Statistical analysis was done using SPSS software version 17.0. Patient completed the VAS in the presence of doctors who were available to assist if necessary. The patient self reported level of education was recorded and categorized into low (less than 10 years of education), intermediate (between 10 and 12 years of education), and high (more than 12 years of education). A random numbered table, from 1-60,

which indicated the total number of participants, was used to randomly allocate each of the participants to either of the midazolam or clonazepam groups. Participants with odd number received clonazepam and even number received midazolam.

Results

In this observational descriptive study, 60 (30 in each group) patients were taken. The mean age of the group midazolam and clonazepam are 40.42 and 41.5 years respectively (Table I). Anxiety reduction from baseline to preprocedure was found to be statistically significant in clonazepamgroup. While evaluating mean anxiety reduction only, mean reduction is greater in the clonazepam group compared to that of midazolam. (Table II). Anxiety reduction was defined as the absolute difference in VAS score between baseline and preprocedure. Patients receiving midazolam were found to be little more anxious, less tranquil than clonazepam. Sedation level was less achieved with midazolam (Table III). In the clonazepam group, greater number of patients could not recall preoperative events. In midazolam group, greater number of patients could recall the same preoperative events.(Table IV). Adverse drug effects were uncommon in participants premedicated with clonazepam (3.3%, 1/30). In contrast a substantial number of participants premedicated with midazolam (23.33%, 7/30) experienced one or more side effects like drowsiness, dizziness, low peripheral oxygen saturation, physical agitation (Figure 1).

Table I: Demographic data of the patients under study (N=60)

Variables	Midazolam Group (n=30)n (%)	Clonazepam Group (n=30)n (%)
Male	12 (40)	13 (43.33)
Female	18 (60)	17 (56.66)
ASA grade I	17 (56.66)	19 (63.33)
ASA grade II	13 (43.33)	11 (36.66)
	(mean±SD)	(mean±SD)
Mean age (in years)	40.42±9.85	41.50±8.32
Mean weight (in Kg)	57.33±6.31	58.62±5.13
Types of surgery	n (%)	n (%)
Cholecystectomy	14 (46.66)	16 (53.33)
Appendicectomy	06 (20)	04 (13.33)
Septoplasty	03 (10)	04 (13.33)
Mastectomy	01 (3.33)	00
Gastrojejunostomy	01 (3.33)	00
Subtotal thyroidectomy	02 (6.66)	04 (13.33)
Tonsillectomy	03 (10)	02 (6.66)

Table II: Prevalence of anxiety in patients under study (N=60)

Variable	Midazolam Group (n=30)(mean±SD)	Clonazepam Group (n=30)(mean±SD)
VAS Baseline	4.2±2.4	4.1±2.6
VAS preprocedure	3.4±2.3	3.0±2.1
P-value	0.48	0.04
P-value		<0.05

Table III: Assessment of sedation in patients under study (N=60)

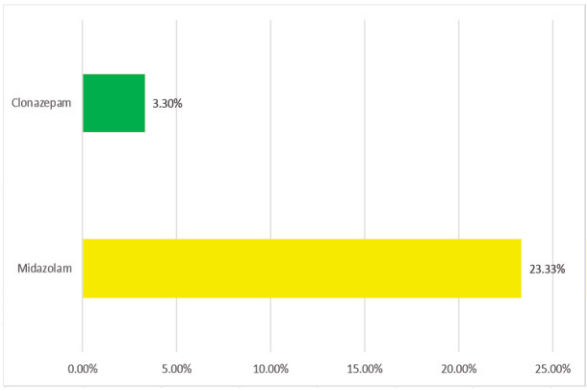
Sedation level	Midazolam Group (n=30) n (%)	Clonazepam Group (n=30) n (%)
1	11 (36.66)	00
2	14 (46.66)	22 (73.33)
3	05 (16.66)	06 (20.00)
4	00	02 (6.66)
P-value	<0.05	

Table IV: Assessment of anterograde amnesia in patients under study (N=60)

Assessment of anterograde amnesia	Midazolam (n=30)		Clonazepam (n=30)	
Preoperative events	Yes n (%)	No n (%)	Yes n (%)	No n (%)
Being taken into operation theatre	21 (70)	09 (30)	08 (26.66)	22 (73.33)
Being shifted from stretcher to operation table	23 (76.66)	07 (23.33)	10 (33.33)	20 (66.66)
Being shown operation theatre under surgical light	21 (70)	09 (30)	11 (36.66)	19 (63.33)

P value <0.05

Figure I: Incidence of adverse drug effects for different premedications (N=60)



Discussion

Benzodiazepines compounds fall into three major categories: long acting compounds- diazepam, chlordiazepoxide, chlorazepate, flurazepam, halazepam, and prazepam; intermediate acting compounds- clonazepam, lorazepam, quazepam, and estazolam; and short acting compounds- alprazolam, oxazepam, temazepam, midazolam, and triazolam. Clonazepam is a benzodiazepine anticonvulsant that has been available for clinical use since 1973. Among adults, clonazepam is metabolized primarily by hydroxylation, although this metabolic pathway generally is impaired in the newborn. The half life in adult is 20-60 hours.[13] Midazolam is rapidly absorbed (peak within 20 minutes) and clonazepam (peak within 30-40 minutes). Bala et al. observed that preoperative single dose of clonazepam 2 mg is a better premedication than 10 mg of midazolam in relieving anxiety and better sedation score with longer duration of action which is beneficial especially in patients staying1-2 days in hospital post-operatively.[14] They also found that patients undergoing elective abdominal hysterectomies under spinal anaesthesia, have significantly lower HAM (Hamilton Anxiety Scale) scores and longer duration of action in clonazepam group compared to midazolam group. It was concluded from their study that midazolam and clonazepam significantly reduce the patient's anxiety without altering the intraoperative haemodynamics. But clonazepam found to be better anxiolytic than midazolam.[14] Our studyhad similar findings but the doses of the premedicants were different. Kumar et al. found that buccal clonazepam demonstrated equivalence to I/V midazolam in controlling acute breakthrough seizure.[15] When extrapolated to domiciliary setting it is likely to be safe option with capability of decreasing status episodes, hospitalization and thus reducing economic burden and psychological stress to the family.[15] Zamiriet al. conducted a randomized double blind controlled trial on clonazepam for the management of anxiety associated with oral surgery.[16] 60 patients were randomly allocated to either a single 2 mg dose of clonazepam or a placebo one hour prior to the surgery. The participants and the outcome assessors were blind to the intervention. Levels of anxiety were recorded using Visual Analogue Scale (VAS) and measuring blood pressure, pulse rate and arterial oxygen saturation percentage. All anxiety determinants (VAS, BP, pulse rate and oxygen saturation) changed significantly one hour after the administration of clonazepam ($p<0.05$). They concluded that clonazepam is an effective anxiolytic drug with minimal side effects which can be used to reduce anxiety in dental patients.[16] Kazemisaeid et al. conducted a placebo controlled double blind randomized controlled trial, which showed a significant increase in anxiety reduction (measured in VAS score) in 151 patients premedicated with intravenous midazolam compared with both diazepam with intramuscular promethazine and a placebo.[17] However, this could possibly be attributed to the fact that patients with higher preprocedural anxiety were premedicated with midazolam, rather than the anxiolytic effect of midazolam itself. Additionally they did not report an increase of side effects in patients premedicated with midazolam.[17,18] Kandel et al. while examining mean anxiety reduction between two groups (diazepam and midazolam), showed that midazolam has higher mean reduction value from baseline at various time periods.[19] Midazolam showed better antianxiety effect and sedative effect compared to diazepam. The study also showed that intramuscular midazolam rapidly produces an appropriate degree of sedation and better quality of sedation than diazepam in patients awaiting surgery. They also showed that midazolam produces better anterograde amnesia than diazepam. But in that study, diazepam was given orally and midazolam was given intramuscularly.[19] Grant et al., Ahn et al., and Mijderwijk et al. described reduced PONV (post-operative nausea and vomiting) after perioperative administration of midazolam. These effects may improve the quality of recovery.[20-22] Earlier studies reported beneficial effects of non pharmacological interventions to reduce

periprocedural anxiety. In three small randomized controlled trials, beneficial effects were seen on periprocedural self reported anxiety in patients who received massage and/or guided imagery prior to the procedure. Similarly a compilation of relaxing music provided by an audio pillow was associated with lower anxiety levels in the time period around the procedure. Finally two small studies showed possible positive effects aromatherapy as well as mindfulness based interventions of anxiety. We did not study these effects, and it is difficult to compare these effects with premedication stratigies.[23-26]

Study limitations

The intervention was not placebo controlled and blinded to neither clinicians nor patients. Additionally, sample sizes were small. Consequently the clinical relevance remains undetermined and further studies are necessary to confirm potential benefits between the two commonly used benzodiazepines.

Conclusion

The standard administration of clonazepam before procedure provides patients with a moderate reduction of periprocedural anxiety. Costs are low and side effects are negligible. Therefore, in our opinion standard prophylactic use of clonazepam seems fair. Midazolam is less effective in reducing preoperative anxiety and premedication of midazolam is associated with a high incidence of adverse effects. Therefore, this study does not support the routine use of midazolam as premedication to reduce anxiety.

Disclosure

There is no conflict of interest.

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Correlation of Serum Manganese Level with Fasting Serum Glucose and Glycated Hemoglobin Levels in Patients with Type 2 Diabetes Mellitus

Eva H[1], Akter QS[2], Alam MK[3]

Abstract

The link between higher glycemic status and increased diabetes-related complications in people with type 2 diabetes mellitus has been known. The aim of the study was to explore the correlation of serum manganese (Mn) level with fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) levels in patients with type 2 diabetes mellitus. A cross sectional study was carried out in the Department of Physiology at Dhaka Medical College in Dhaka from July 2014 to June 2015, also in collaboration with the Department of Biochemistry at Bangladesh Institute of Research for Diabetic Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka. A total of 100 subjects were included in this study, among them 50 were diagnosed diabetes mellitus patients ranging in age from 40 to 55 years old and 50 were healthy subjects of similar ages and BMI as control group. Serum manganese was measured by flame atomic absorption spectophotometry. The unpaired Student's't' test and Pearson's correlation coefficient (r) test were used for statistical analysis by SPSS windows package, version 20. In this study, mean manganese level was significantly lower ($P<0.001$) in patients with type 2 diabetes mellitus than that of control group. On correlation analysis, serum Mn level showed significant negative correlation with FPG and HbA_{1C} levels in patients with type 2 diabetes mellitus. The study reflected that serum Mn level was reduced in diabetes mellitus with higher glycemic status.

Key words: Serum manganese, fasting plasma glucose, HbA_{1C}, type 2 diabetes mellitus.

Introduction

Diabetes mellitus (DM) is a metabolic condition caused by either a complete lack of insulin or a decrease in tissue insulin sensitivity.[1] According to the International Diabetes Federation (IDF), about 425 million individuals had diabetes in 2017, and this number is expected to climb to 629 million by 2045. In the year 2017, 6.9 million people in Bangladesh had diabetes.[2]

Recent research has looked into the link between glycaemic control and trace micronutrients such as manganese.[3] Manganese (Mn) functions as a cofactor for antioxidant enzymes such as superoxide dismutase, which aids in the removal of free radicals.[4] Diabetes results in increased urine excretion and a reduction in Mn levels in the blood. Manganese deficiency increases oxidative stress, which leads to diabetes complications.[5] The oxidation of low density lipoprotein (LDL) cholesterol was less protected in diabetes with lower Mn levels. The production of intra-arterial plaque is aided by LDL oxidation, which can lead to heart attacks and strokes.[6]

Lower serum manganese levels clearly enhance the risk of diabetic complications in people with type 2 diabetes mellitus. The goal of this study was to look into Mn status and how it changed with glucose status in patients with type 2 diabetes mellitus.

Material and Methods

This cross-sectional study was conducted in the

1. Dr. Hossneara Eva. Associate Professor and Head, Department of physiology, Brahmanbaria Medical College, Brahmanbaria.
Email: hossnearaeva@gmail.com
2. Dr. Quzi Shamima Akter. Ex-Professor and Head, Department of Physiology, Dhaka Medical College, Dhaka.
3. Dr. Md. Khairul Alam. Professor and Head, Department of Physiology, Army Medical College Cumilla.

Department of Physiology Dhaka Medical College, Dhaka from July 2014 to June 2015. The protocol for this study was authorized by Ethical Review Committee of Dhaka Medical College and Diabetic Association of Bangladesh. For this study, 50 type 2 diabetes patients (28 male and 22 female) with FPG levels ≥ 7.0 mmol/l and HbA_{1C} ≥ 6.5 percent were recruited from the outpatient department of BIRDEM General Hospital in Dhaka, and 50 age and BMI matched healthy volunteers (26 male and 24 female) served as controls. Following subject selection, the nature, goal, and usefulness of the study were thoroughly explained to each subject, and informed written consent was obtained. Before drawing blood, a thorough medical and family history was collected. The individuals' anthropometric measurements and blood pressure were taken. A data schedule was used to keep track of everything. A disposable plastic syringe was used to collect 5 mL of venous blood from each subject's antecubital vein for estimate of biochemical assays. HbA_{1C} and FPG levels were measured in the Department of Biochemistry at the BIRDEM General Hospital in Dhaka. Serum manganese (Mn) level was measured by using flame atomic absorption of spectrophotometer in spectrophotometric method in the laboratory of the Atomic Energy Centre's Department of Chemistry in Dhaka. The unpaired Student's't' test and the Chi square test were used for statistical analysis. The level of significance was set at a P value of less than 0.05. The statistical analyses were carried out using the SPSS Version 20 computer-based statistical tool.

Results

Table I displays general characteristics. Patients with diabetes mellitus had a significantly reduced mean serum manganese level ($p< 0.001$) in this study (Table II). The level of serum manganese had a statistically significant negative correlation with the level of FPG (Table III). Again, Serum manganese levels were found to have a statistically significant negative correlation with $HbA1_C$ levels (Table III).

Table I: General characteristics of the subjects in both groups (n=100)

Parameters	Control (n=50)	Diabetic patients (n=50)	p value
Age (years)	47.58±3.59 (40.00-52.00)	48.00±3.49 (42.00-53.00)	0.554
Sex			
Male	26 (52.0)	28 (56.0)	
Female	24 (48.0)	22 (44.0)	
Height (cm)	159.54±5.20 (150.00-168.00)	158.32±8.17 (140.00-178.00)	
Weight (kg)	64.62±5.51 (50.00-78.00)	64.54±8.21 (50.00-80.00)	
Body mass index (kg/m^2)	25.44±2.06 (20.58-30.86)	25.80±3.06 (20.14-33.78)	0.487
Systolic blood pressure (mmHg)	121.70±5.31 (110.00-130.00)	123.40±7.45 (110.00-140.00)	0.799
Diastolic blood pressure (mmHg)	76.30±5.70 (70.00-85.00)	79.70±5.19 (70.00-90.00)	0.498

Sex distribution has been shown in number and percentage. All other results are expressed as mean±SD. Figures in parentheses indicate range. Unpaired Student's "t" test was performed to compare between groups. The test of significance was calculated and p value < 0.05 was accepted as level of significance.

Table II: Study parameters of the subjects in both groups (n=100**)**

Parameters	Control (n=50)	Diabetic patients (n=50)	p value
Fasting plasma glucose (mmol/L)	5.18±0.30 (4.30-5.80)	10.06±2.18 (6.90-14.00)	<0.001***
HbA_1c (%)	5.17±0.28 (4.80-6.00)	9.04±1.60 (6.80-13.70)	<0.001***
Serum manganese (ng/ml)	12.95±2.76 (8.07-18.89)	10.45±2.77 (6.63-16.40)	<0.001***

Results are expressed as mean±SD. Unpaired Student's 't' test was performed to compare between groups. ***P< 0.001. n = Number of subjects.

Table-III: Correlation of fasting plasma glucose level (FPG) and glycated hemoglobin (HbA1c) levels with serum manganese level in study group (n=50)

Parameter	r	p
FPG	-0.308	<0.05*
HbA1c	-0.384	<0.01*

Pearson's correlation-coefficient (r) test was performed to compare relationship between parameter. The test of significance was calculated and p value <0.05 was accepted as level of significance. n = Number of subjects. * = Significant.

Discussion

In the present study, age and BMI of all the subjects in both groups were almost similar and statistically no significant differences were observed between them. So, they were matched for age and BMI. Again, the mean systolic and diastolic blood pressure was almost similar and statistically no significant differences in patients with type 2 diabetes mellitus and healthy subjects. Again, in the present study, the mean serum manganese level was lower in type 2 diabetes mellitus patients than that of healthy subjects and the result was statistically significant.[6,7]

In the present study, Pearson's correlation (r) test was done to observe the relationship of FPG level with serum manganese level in study group. FPG level showed negative correlation with serum manganese level which was statistically significant in patients with type 2 diabetes mellitus.[6,7,8]

Again, Pearson's correlation (r) test was done to observe the relationship of HbA_{1C} level with serum manganese level in study group. HbA_{1C} level showed negative correlation with serum manganese level and the relationship was statistically significant. Similar findings were observed by researchers from several countries.[6,7,8] However, a small number of researchers found no significant differences in serum manganese levels in type 2 diabetes mellitus patients.[9,10]

Hyperglycemia is the diagnostic hallmark finding in patients with type 2 diabetes mellitus.Furthermore, a large majority of diabetes mellitus patients have low serum manganese levels. Literature review suggested that prolonged hyperglycemia in uncontrolled diabetes causes raises the osmotic pressure in renal tubules, which prevents the kidney from reabsorbing water, leading in polyuria. Due to this polyuria increased excretion of manganese in patients with type 2 diabetes mellitus.[11,12,13,14] As a result serum manganese level was reduced in diabetes mellitus.[6]

In this study, higher levels of FPG and HbA_{1C} in patients with type 2 diabetes mellitus with lower serum manganese are suggestive of risk factors for development of diabetes related complications[6].

Conclusion

The study reflected that serum Mn level was lower in patients with type 2 diabetes mellitus with was higher glycemic status.

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Conflict of Interest: None

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Acknowledgements

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As principal investigator Dr

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