

A Comparative Study to Evaluate the Role of Teriparatide in Post-Operative Intertrochanteric Fracture Healing

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Submitted: 16 Jan 2023; Accepted: 24 Jan 2023; Published: 31 Jan 2023

Citation: Singh, A., Patel, S., Jha, K. A., Singh, S. K., Chaubey, A. (2023). A Comparative Study to Evaluate the Role of Teriparatide in Post-Operative Intertrochanteric Fracture Healing. *Int J Ortho Res*, 6(1), 01-08.

Abstract

Background: Intertrochanteric fractures result in serious health problems and decrease health-related quality of life (HRQoL) in geriatric population. Faster time-to-union is important for early return to daily activities and reduction of complications. Teriparatide has been shown to accelerate fracture-healing. Purpose of the present prospective study was to evaluate the effect of teriparatide on the course of intertrochanteric fracture-healing.

Methods: 40 patients of intertrochanteric fractures who underwent surgical intervention between October 2020 and September 2021 were enrolled in this prospective study and followed for minimum of six months. Group A included patients who received teriparatide along with calcium supplementation; patients in Group B received only calcium supplementation postoperatively. Demographics, time-to-union, VAS score, mortalities, and radiographic and functional outcomes between groups were compared.

Results: A significantly shorter time-to-union was found in the teriparatide-treated groups (mean, 9.2 v/s 12 weeks, [P=0.00001]). Regard to Harris hip score [HHS], were significantly better in teriparatide-treated groups at 1 month (mean 79.16 v/s 69.76) [P=0.001] and 6 month (mean 84.1 v/s 75.6) [P=0.001]. Similar inter-group differences were noted when comparing the pain VAS scores at 1 month (mean 2.4 v/s 2.9) [P=0.005], 3 month (mean 2.05 v/s 2.75) [P=0.001] and 6 months (mean 0.0 v/s 0.35) [P=0.01] and also significant effectiveness regards to Parker and Palmer mobility score at 1 month (mean 6 v/s 4.3) [P=0.001], 3 month (mean 6.9 v/s 5.3) [P=0.001] and 6 month (mean 8.7 v/s 6.8) [P=0.001] and Pre BMD score (mean -2.3 v/s -3.2) [P=0.16] and 3 month (mean -2.2 v/s -2.1) [P=0.46] and at 6 month (mean -1.11 v/s -1.4) [P=0.016].

Conclusions: Teriparatide shows faster fracture healing and better functional outcome and decreases the pain in the intertrochanteric fracture patients. However, a randomized, large-scale cohort study is still necessary to determine the efficacy of teriparatide in intertrochanteric fractures.

Keywords: Intertrochanteric fracture, Teriparatide injection.

Introduction

Intertrochanteric fracture is common in geriatric population but it is not uncommon in younger age group. Intertrochanteric fracture is mostly due to trivial trauma. Incidence varies from country to country [1]. The total number of hip fractures worldwide will reach 2.6 million by 2025 and lifetime risk at 50 years of age of 5.6% for men and 20% for women [2, 3]. The risk factors for hip fractures are individuals with osteoporosis and any medical conditions associated with bone loss like Diabetes mellitus, Hypothyroidism, Hyperthyroidism and Cushing's syndrome. The

primary goal of treatment is early mobilization and prevent complications like thromboembolism, decubitus ulcer, functional loss, poor health-related quality of life and higher mortality rate and are achieved by open reduction and internal fixation [4-6]. Early time to fracture union is achieved by early return to daily activities and to avoid complications in old patients remains a problem for surgeons [7-8].

Various operative procedures with different implant have been used for treatment of intertrochanteric fractures like sliding hip

screws or trochanteric nail. Collapse of femoral neck, loss of hip offset and shortening of the leg are problem with sliding hip screws, although too much shortening result in poor hip function therefore a new intramedullary device like Proximal Femoral Nail was designed in 1996 which gives an advantage of minimally invasive surgery [2].

Intramedullary devices such as proximal femoral nail (PFN), are more stable than sliding hip screws which works on principle of loading with a shorter lever arm, as the distance between the hip joint and the nail is reduced compared with that for a plate, thus diminishing the deforming forces across the implant. Intramedullary devices are indicated particularly in unstable trochanteric and subtrochanteric fractures because of their biomechanical advantage than plate [7].

Although data are less as there is an interest in using systemic medical interventions to potentially accelerate the fracture repair. Intermittent administration of human recombinant parathyroid hormone (PTH) (1-34) (Teriparatide) is an FDA-approved anabolic treatment used to treat osteoporosis in men as well as in women after menopause. It slows down the rate at which bone is broken down in your body and maintains the bone mineral density and reduces your risk of fracture. It works by increasing the number and activity of bone-forming cells (osteoblasts) and this strengthens the bones and minimizes the fracture risk as it hastens the fracture healing as there are few randomized controlled studies at present.

Material and Methods

After taking clearance from the ethical committee the study was conducted in the Dept. of Orthopaedics, Apex hospital Varanasi according to inclusion and exclusion criteria. If patient meets all the required inclusion criteria, then written informed consent was obtained from all the patients or their family for participation in the study. For this study we recruited 40 patients of intertrochanteric fracture presented to our hospital between October 2020 to September 2021 and followed for minimum six months. After enrolment patient was randomized into two groups (A and B) as:

GROUP A: 20 patients of post-operative intertrochanteric fracture treated with PFNA2 receiving subcutaneous injection of teriparatide 20mcg daily.

GROUP B: 20 patients of post-operative intertrochanteric fracture treated with PFNA2 not receiving injection of teriparatide.

Rest anti osteoporotic treatment remains similar in both groups (e.g., Oral Calcium supplement and Vit D)

Patient was explained in detail about the study and was enrolled after taking a written consent. Patient not willing for same was excluded from the study.

The primary objective of the study was to evaluate the difference in rate of fracture union amongst post-operative intertrochanteric

fracture patients with or without teriparatide therapy. Since the study was time bound, all consecutive patients meeting the eligibility criteria during the study period were enrolled. It was expected from the previous experience that 20 per group would be enrolled and the sample size was calculated

On admission to the institution, thorough history about mode of injury, associated injuries, previous medical and surgical history and pre-trauma ambulation were documented for each patient. Clinical examination, neurovascular status and radiological assessment of the fractured limb was done. The injured extremity was splinted in a Thomas splint with skin traction. Patients were investigated further depending on the general condition and co-morbidity of the patient and routine pre-operative protocol was followed as per our hospital guidelines.

Preoperatively radiographic examination of the affected hip in antero-posterior (AP) view of pelvis and lateral views and were classified according to AO classification for proximal femur fracture. Osteosynthesis with intramedullary device was chosen as it is the standard treatment for fixation of intertrochanteric fractures in our institute. In our study we used proximal femoral nail (PFN) as intramedullary implant. In order to minimize the implant related confounding factors patients treated with extramedullary devices such as dynamic hip screw (DHS) was not included in this study. To minimize drug related variables, patients who were taking antiresorptive drugs prior to fracture were excluded. Patients were operated following the surgical principles including fracture reduction and Tip apex distance (TAD). Group A patients received calcium supplementation postoperatively and Group B patients were advised to take daily subcutaneous injections of 20 micro gram teriparatide for 6 months starting from 2nd post op day along with calcium supplementation.

Follow Up

Patients were followed at 2 weeks of surgery for stitch removal and clinical assessment, at 4 weeks and then at 4 weeks interval till 6 months. During the follow up radiographic examinations done including anteroposterior (AP) view of pelvis, AP and lateral views of the affected hip at 4 weeks and then at every follow up visit until fracture united. Assessment of functional status done by Parker and Palmer hip mobility scoring at 6 months post op and assessment and analysis of any complications observed.

Fracture union was defined as recanalization of the trabeculae or visible bridging callus on both radiograph views; delayed union is defined as no signs of fracture healing for 24 weeks; and non-union is defined as the absence of bone union 36 weeks postoperatively [7]. The tip-apex distance was measured using AP and lateral radiographs of the affected hip [7].

Statistical Method

Analysis was done by SPSS software of version 17.0 (SPSS, Chicago, Illinois). Continuous variables are presented as mean \pm SD, and categorical variables are presented as absolute numbers and percentage. Chi square test or Fisher's exact test were used to ana-

lysed the categorical variables and normally these categorical variables were compared using the unpaired t test. A 'P' value of less than 0.05 was taken to indicate a significant difference.

Results

The study consists of 40 patients of intertrochanteric fractures treated with intramedullary nailing (Proximal femoral nail) divided into 2 groups of 20 each. Post operatively, 20 patients (Group A) were given only calcium and other 20 patients (Group B) were given Teriparatide therapy along with calcium.

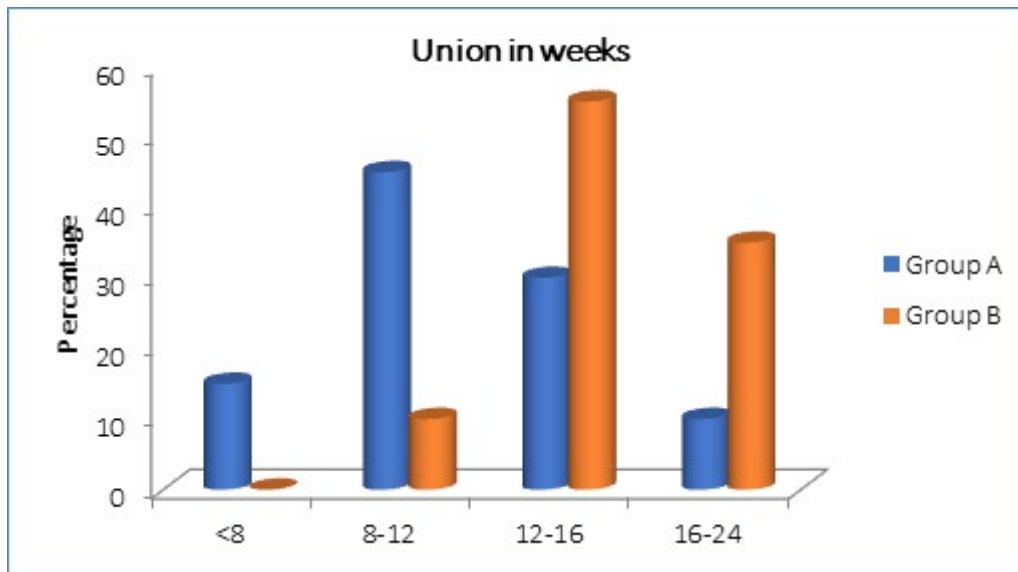
Average age of patients with intertrochanteric fractures was 70 years. It was found that age distribution between the two groups was comparable and there was no statistically significant difference between two groups. Majority of patients in our study were females (27 out of total 40 patients =65%) and rest 13 patients were male. In group A, 75% (15) of patients were females while in group B, 80% (16) of patients were females. The difference in gender distribution in between two groups was not significant (Table 1).

Age groups years	Group A		Group B		P value
	No.	%	No.	%	
<50-60	2	10.0	4	20.0	0.904
61-70	10	50.0	8	40.0	
71-80	6	30.0	5	25.0	
>80	2	10.0	3	15.0	
Gender					
Female	14	70.0	13	65.0	1.000
Male	6	30.0	7	35.0	
Total	20	100	20	100	

Out of 40 patients, 36 were due to simple fall, 2 were due to fall from height and 2 were due to road traffic accident. All of them were closed injury. The distribution in two groups was also comparable. We classified Intertrochanteric Fracture according to the AO Group Classification. Maximum numbers of patients were classified in Group A2 (28 patients out of 40). The distribution of the fracture pattern in between two groups was comparable and there was no significant difference in between the groups.

In our prospective study, union time in majority of the patients of Group A (45%) was --8-12weeks while in majority of the patients of Group B (55%), it was less, i.e., 12-16 weeks. It was found that the difference in fracture union time between two groups was statistically significant (Table 2).

Union in weeks	Group A		Group B		P Value
	No.	%	No.	%	
<8	3	15	0	0.0	0.00001
8-12	9	45	2	10	
12-16	6	30	11	55	
16-24	2	10	7	35	
total	20	100	20	100	



In some patients, we observed complications which were either related to surgery, implant related or fracture healing. Pulling out of screw from neck was observed in one patient of group A. Post op shortening of 0.5 - 1.5cm was found in 4 patients of Group A and 3 patients of Group B. Varus collapse was seen in 2 patients of Group A. Overall, the difference in complications between two groups was not statistically significant.

Parker and Palmer Mobility Scores At 6 Months

In our study, mean mobility score at 6 months in Group A came out 8.7, while in Group B mobility score was 6.85. The difference of the Parker mobility score at 6 months between the two groups was statistically significant (Table 3).

	Group A (Mean+/-SD)	Group B (Mean+/-SD)	P Value	
Parker and palmer mobility score	8.70±0.923	6.85±0.98	<0.001	Significant

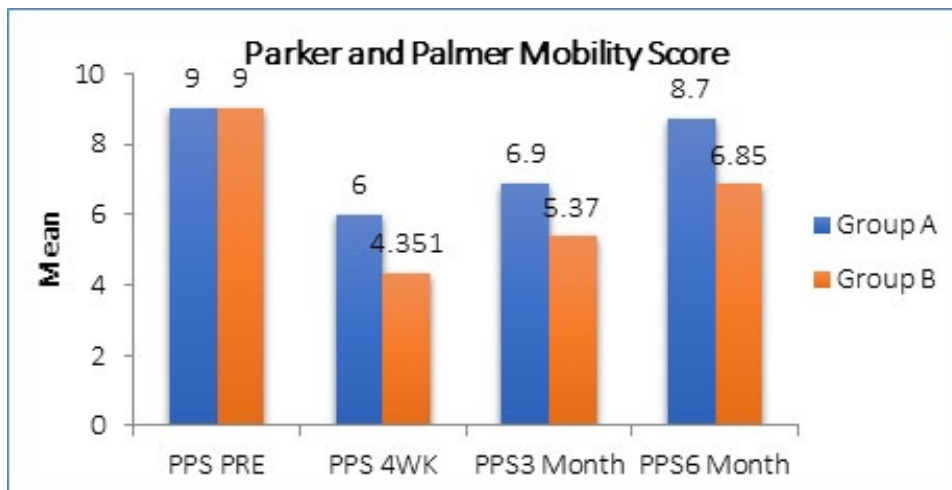


Table 4: DEXA Scan shows no statistical significant difference was noted preoperatively and at 3 month in group A and group B. Band was found to be significant at 6 month with P value at pre op , 3 month and 6 month is 0.166,0.462 and 0.016 respectively.

DEXA	Group A Mean±SD (N=20)	Group B Mean±SD (N=20)	p-value
DEXA PRE	-2.340±2.2027	-3.230±1.7610	0.166
DEXA 3M	-2.290±0.8559	-2.140±0.2891	0.462
DEXA 6M	-1.110±0.5360	-1.480±0.3736	0.016

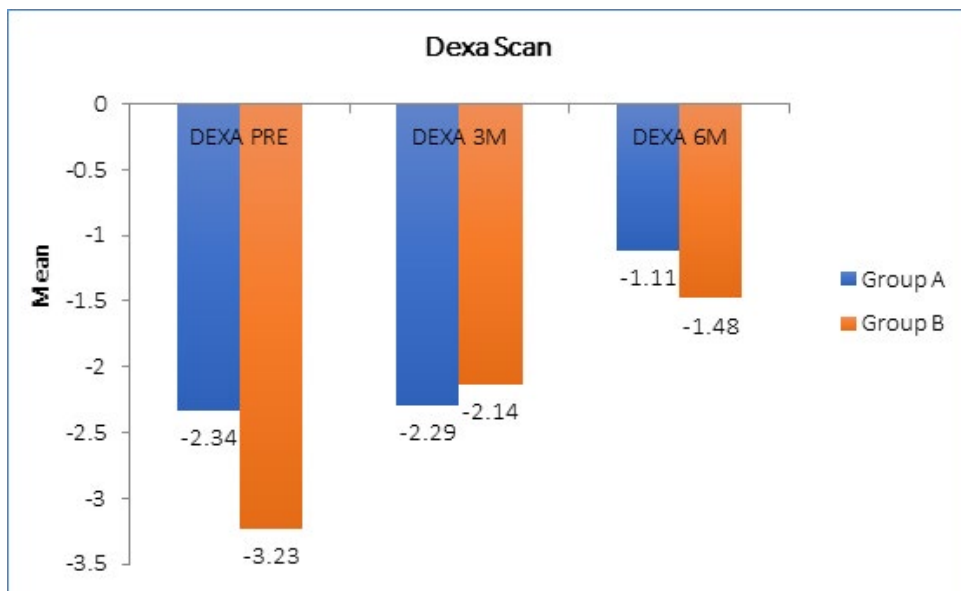


Table 5: Harris hip score:

	Group A Mean±SD N=20	Group B Mean±SD N=20	p-value
HHS PREINJURY	73.215±6.3004	73.426±10.3508	0.938
HHS 4WK	79.16±4.85	69.763±5.5136	<0.001
HHS 6M	84.184±3.0425	75.604±6.9924	<0.001

Table 5: Shows HHS in group A pre injury, 4 week, 6 month shows mean value as 73.215±6.3004, 79.16±4.85 and 84.184±3.0425 and in group B 73.426±10.3508, 69.763±5.5136 and 75.604±6.9924 with P value found to be significant <0.001

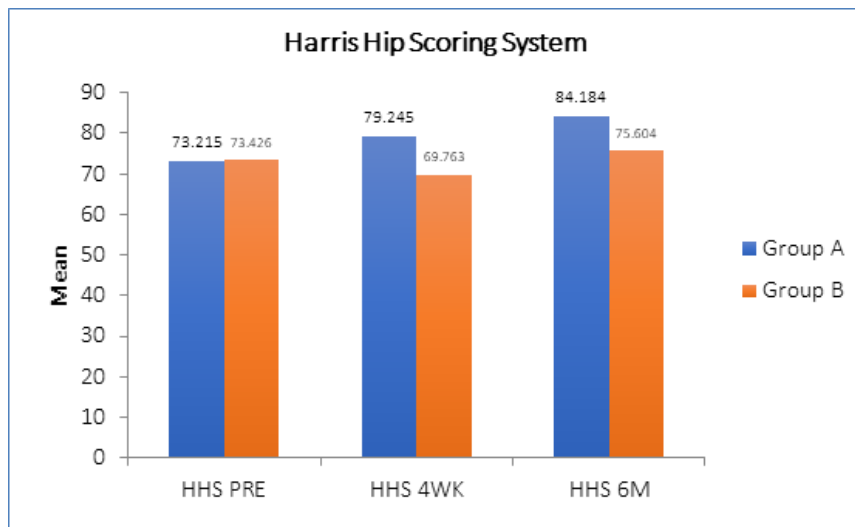
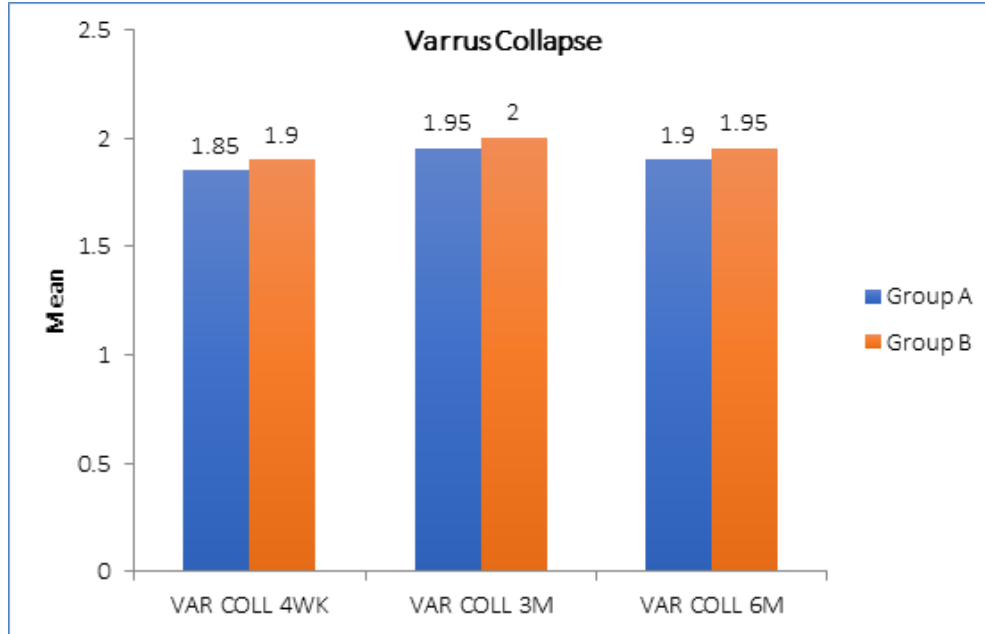


Table 6: Varus collapse:

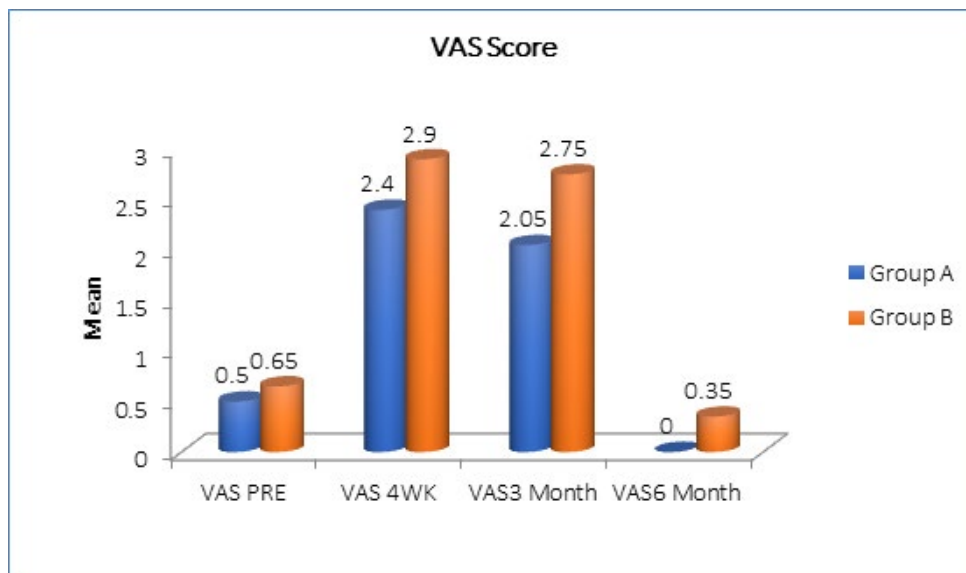
	Group A Mean±SD N=20	Group B Mean±SD N=20	p-value
VAR COLL 4WK	1.85±0.366	1.90±0.308	0.643
VAR COLL3M	1.95±0.224	2.00±0.000	0.324
VAR COLL6M	1.90±0.308	1.95±0.224	0.560

Table 6: Varus collapse shows mean value in group A and B was found to be insignificant.



VAS Score	Group A Mean±SD N=20	Group B Mean±SD N=20	p-value
VAS PRE	0.50±0.607	0.65±0.813	0.512
VAS 4WK	2.40±0.50	2.90±0.55	0.005
VAS3 Month	2.05±0.51	2.75±0.63	0.001
VAS6 Month	0.00±0.000	0.35±0.587	0.011

Table 7: vas score in group A and group B with mean in pre , 4 week , 3 month and 6 month is 0.50±0.607,2.800±0.7678,2.05±0.759,0.00±0.000 and 0.65±0.813,2.950±0.5104,2.45±0.826,0.35±0.587 with mean P value at 4week , 3 month and 6 month is significant<0.001



Discussion

Intertrochanteric hip fractures are the frequent injuries affecting elderly patients with osteoporosis and are a burden for the individual, their family, and the healthcare system [9-10]. Pain and immobility due to these fractures lead to a loss of functioning in daily activities and loss of quality of life and are associated with high morbidity and mortality [11-12]. The primary goals in treating intertrochanteric fractures in these patients are pain relief, improvement of mobilization, and prevention of complications associated with comorbidities. Most of the intertrochanteric fracture or fracture neck of femur require surgical intervention. Increased risk of fall together with decreased bone strength account for the increased risk of fracture with increasing intertrochanteric fractures still carry a mortality rate ranging from 2.49% to 33% at one month to one year and constitute a major socioeconomic problem [9-10].

To date no systemic treatment is approved for healing of the fracture as impaired healing slows the rehabilitation process, which affects the health-related quality of life and at the same time it affects the associated cost and economic burden to both the society and the patients. Early and faster union is important for activity of daily living and reduction of complications as well. This prospective study demonstrated that Teriparatide fastens the fracture union and improves functional outcome in postoperative patients of intertrochanteric fracture and there was significant difference in between the two groups.

Previously, Teriparatide appeared effective in improving BMD and reducing the rate of subsequent osteoporotic fracture [13]. In past 20 years, many studies on animals and humans have been done regarding role of Teriparatide in fracture union [14-15]. Only a few studies have been done in India on clinical use of teriparatide in fracture healing, where cost is a major factor. The study done at our institute was a prospective design comprising of 40 patients, of them 27 were females and 13 were males (1.85:1) which was comparable to other studies on intertrochanteric fractures like Gardenbroek et al, Simmermacher et al. (3.3:1) [16-17].

Significant female dominance may be attributed to the fact that osteoporosis sets in after menopause in many females and proximal femoral fractures are on rise. The average age of the patients having intertrochanteric fracture in our study was 70 years which was comparable to other studies like Gardenbroek et al (79.1 yrs) and Simmermacher et al (80.6yrs) [16-17]. Majority of patients in our study sustained a fracture due to minor trauma, which is in accordance with other major studies. This may be attributed to poor bone quality in the elderly patients, loss of mental faculties and high stresses in the proximal femur region.

In our study majority of patients were in A2 group of AO classification which was classified into 3 groups. This trend of maximum patients in the A2 group is consistent with the international studies like Gardenbroek et al and Simmermacher et al. [16-17]. This may be due to the inherent geometry and stress pattern of the proximal femur.

In our study, we analysed that Teriparatide has significantly reduced the time of fracture healing and improved the functional outcome at 6 months compared with that in the control group of patients given only calcium replacement therapy. Huang TW et al in their study also analysed that union time was significantly reduced in teriparatide treated group [18]. Lau et al in their study concluded that patients who were treated with teriparatide had statistically significant difference in radiological fracture healing time compared with the control group [19]. The overall complication rate was not significantly different in two groups. In our study, there was a significant difference in the mobility scores in between two groups and showed better functional outcome in teriparatide treated group. Similar results were shown in study by Huang et al. [18].

As teriparatide therapy can promote osteoporotic fracture healing and improve function outcome, we suspect that teriparatide may prove to be useful in the stimulation of implant anchoring and fixation. It may be useful in high risk of delayed or non-union.

Limitations

In this study must be acknowledged. In our study duration and sample size was small. In view of very limited studies on the role of teriparatide in fracture healing of intertrochanteric fractures, the outcome could not be compared with literature. All the patients in our study were treated by proximal femoral nailing. We do not know whether the adding of teriparatide could also benefit the patients treated with extramedullary implant like dynamic hip screw. The strict inclusion criteria for this study were designed to limit the variables in the study, but it also reduced the numbers of subjects and limited the power of the study to detect a clinically significant difference.

Conclusion

Teriparatide shows faster fracture healing and better functional Outcome and decreases the pain in the intertrochanteric fracture patients. The faster union important for elderly patients with intertrochanteric fractures to enable them to return to daily activities and reduce morbidity and mortality. However, a randomized, large-scale cohort study is still necessary to determine the efficacy of teriparatide in intertrochanteric fractures.

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