

Healing of intertrochanteric femur fractures by teriparatide: Our experience from Karnataka

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Abstract

Background: Proximal femoral fractures due to osteoporosis have a huge impact on medical problems and health care system.¹⁻² Osteoporotic hip fractures carry high complication rate and high mortality. **Objective:** To assess the difference in rate of fracture union among post-operative intertrochanteric fracture patients with or without Teriparatide therapy. **Methodology:** This is a randomized controlled study conducted at Department of Orthopaedics, Navodaya medical college and research center, Raichur. Subjects in the age group of 50-80 years having intertrochanteric fracture were included. Patients divided into two groups. Group A patients received only calcium supplementation postoperatively. Group B patients were given teriparatide therapy along with calcium supplementation. Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, Illinois). **Results:** Average age of patients with intertrochanteric fractures was 76 years. Majority of patients in our study were females (30 out of total 40 patients =75.0%) and rest 10 patients were male. In group A, 75% (15) of patients were females while in group B, 75% (15) of patients were females. In our prospective study, union time in majority of the patients of Group A (55%) was 12-16 weeks while in majority of the patients of Group B (45%), it was less, i.e. 8-12 weeks. **Conclusion:** Study shows faster fracture healing statistically significant in the intertrochanteric fracture patients treated with teriparatide therapy.

Key Word: Intertrochanteric fracture, femur, teriparatide

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INTRODUCTION

Proximal femoral fractures due to osteoporosis have a huge impact on medical problems and health care system.¹⁻² Osteoporotic hip fractures carry high complication rate and high mortality. Which adversely effects outcomes on geriatric populations³⁻⁶. Osteoporotic hip fractures in many patients leads to poor health related quality of life significant functional loss and higher mortality rate.⁷⁻⁹ So fast union is important for daily activity and reduction of complication. Usually surgery is indicated, but pain relief, early weight-bearing and an early return to daily activities is of critical importance to

avoid complications in geriatric patients remains a challenge for orthopaedic surgeons.⁵⁻⁶ Fixation with an extramedullary or intramedullary device is the standard treatment for such fractures but stability of fixation depends on the quality of bone.¹⁰⁻¹¹ Even after achieving good reduction and optimal positioning of the implant, failure rate in osteoporotic bone is higher than those in normal bone because of age-related decreases in bone regenerative capacity and poor bone stock.^{6,12} Recombinant parathyroid hormone (Teriparatide) is the only anabolic medication that has proven efficacy in stimulating bone formation in addition to promoting growth factors production for fracture healing. Studies have shown that Teriparatide can play an important role in the treatment of these fractures.^{5,13-14} In some human trials; it appears to lessen the risk of nonunion and enhance fracture healing.¹⁵⁻¹⁹ So the present study was undertaken to assess and compare the effect of teriparatide on fracture healing in osteoporotic intertrochanteric femur fractures.

MATERIALS AND METHODS

This is a randomized controlled study conducted at Department of Orthopaedics, Navodaya medical college

and research center, Raichur. We selected the eligible patients from orthopedic OPD of Navodaya Medical College and Hospital. For this study 40 patients were selected of intertrochanteric fracture presented to our hospital between December 2017 to November 2018 and followed up for minimum six months.

Inclusion criteria

- Subjects in the age group of 50-80 years having intertrochanteric fracture and willing to participate in study after written consent.

Exclusion criteria

- Patients who are having secondary osteoporosis
- Known allergy to teriparatide,
- Unfit for surgery due to the associated comorbid medical condition
- Patients who are taking any antiresorptive drug like bisphosphonate prior to fracture.

Patients divided into two groups by computer-generated number sequence and were contained in sequentially numbered opaque envelopes to ensure blinding. Two groups (A and B) were made each of twenty patients.

Group A patients: received only calcium supplementation postoperatively

Group B patients: were given teriparatide therapy along with calcium supplementation. Teriparatide administrated by pen-type, subcutaneous injections delivery system. Patients were educated regarding Teriparatide administration method.

Sample size calculation:

The formula for calculated sample size is given below:

$$n = \frac{z_1 - \frac{\alpha}{2} \sqrt{2P(1-P)} + z_1 - \beta \sqrt{(P_1(1-P_1) + P_2(1-P_2))}}{(P_1 - P_2)2}$$

Where P₁ = Anticipated proportion of union rate with teriparatide therapy;

P₂ =Anticipated proportion of union rate without teriparatide therapy;

On admission to hospital we have recorded history about mode of injury, associated injuries, previous medical and surgical history were documented for each patient. Clinical examination, neurovascular status and radiological assessment of the fractured limb was done. The injured extremity was kept in skin traction. Patients were investigated further depending on the general condition and co-morbidity of the patient and routine pre-operative protocol was followed. Preoperatively, all patients had radiographic examinations including antero-posterior (AP) view of pelvis and AP and lateral views of the affected hip. They were explained regarding the illness and post operative complications and informed consent for surgery was taken. Fractures were classified according to AO classification for

proximal femoral fractures. In our study we used proximal femoral nail (PFN) as intramedullary implant as it is the standard treatment for fixation of intertrochanteric fractures in our institute. Other treatment modalities of treatment (extramedullary devices) like dynamic hip screw were not included to minimize the implant related confounding factors. Patients were operated following the surgical principles including fracture reduction and Tip apex distance (TAD). Group A patients received calcium carbonate salt 500 mg per day supplementation postoperatively and Group B patients were advised to take teriparatide daily subcutaneous injections of 20 micro gram for 6 months starting from 2nd post op day along with calcium supplementation.

Follow up: Patients were reviewed in OPD at 15 days of surgery for stitch removal and clinical assessment, at 4 weeks and then at one month 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 operative 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 nonunion is defined as the absence of bone union 36 weeks postoperatively¹¹. The tip-apex distance was measured using AP and lateral radiographs of the affected hip¹¹.

Parker and Palmer hip scoring system: This mobility score consider three specific factors, which include the patient’s ability to ambulate within their place of residence, the ability to ambulate outside, and the ability to go shopping. Independence of walking at 6 months (using Parker and Palmer mobility scoring system) was used for the assessment of functional status in the post operative period (Table 1).

Statistical method: Statistical analysis was performed by the SPSS program for Windows, version 17.0 (SPSS, Chicago, Illinois). Continuous variables were presented as mean ± SD, and categorical variables are presented as absolute numbers and percentage. Data was checked for normality before statistical analysis. Normally distributed continuous variables were compared using the unpaired t test. Categorical variables were analyzed using either the chi square test or Fisher’s exact test. For all statistical tests, a ‘P’ value less than 0.05 was taken to indicate a significant difference.

RESULTS

The study involved 40 patients of intertrochanteric fractures treated with intramedullary nailing (Proximal femoral nail). Subjects were 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.

Table 1: Parker and Palmer hip scoring system

Mobility	No aid	With an aid	With help from another person	Not at all
Able to get about the house	3	2	1	0
Able to get out of the house	3	2	1	0
Able to go shopping	3	2	1	0

Table 2: Distribution and comparison according to Demographic profile of patients

Age groups (years)	Group A		Group B		P value
	Frequency	Percent	Frequency	Percent	
<70	6	30	8	40	0.84 Not significant
71-80	8	40	9	45	
81-90	5	25	3	15	
>90	1	5	1	5	
Gender					
Female	15	75	15	75	1.0
Male	5	25	5	25	Not significant

Average age of patients with intertrochanteric fractures was 76 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 (30 out of total 40 patients =75.0%) and rest 10 patients were male. In group A, 75% (15) of patients were females while in group B, 75% (15) of patients were females. The difference in gender distribution in between two groups was not significant (Table 2). Out of 40 patients, 34 were due to simple fall, 2 were due to fall from height and 4 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 (26 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.

Table 3: Distribution and comparison according to fracture union time

Union in weeks	Group A		Group B		P value
	Frequency	%	Frequency	%	
<8	0	0	3	15	0.008 Significant
8-12	2	10	9	45	
12-16	10	50	7	35	
16-24	8	40	1	5	
Total	20	100	20	100	

In our prospective study, union time in majority of the patients of Group A (55%) was 12-16 weeks while in majority of the patients of Group B (45%), it was less, i.e. 8-12 weeks. It was found that the difference in fracture union time between two groups was statistically significant (Table 3). 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 1.0 - 2.0 cm was found in 6 patients of Group A and 3 patients of Group B. Varus collapse was seen in 3 patients of Group A Overall, the difference in complications between two groups was not statistically significant.

Table 4: Parker and Palmer mobility scores at 6 months

	Group A	Group B	P value
	Mean \pm SD	Mean \pm SD	
Parker mobility score	6.00 \pm 1.50	7.40 \pm 1.32	<0.001 Highly significant

In our study, mean mobility score at 6 months in Group A came out 6.0, while in Group B mobility score was 7.40. The difference of the Parker mobility score at 6 months between the two groups was statistically significant. It means in group B the score is significantly higher as compared to other group.

DISCUSSION

Proximal femoral osteoporotic fractures are frequent injuries affecting elderly patients are a burden for the individual, their family, and the health-care system.³⁻⁴ Pain and prolonged immobility due to these fractures lead to a loss of functioning in day to day activities and loss of quality of life and are associated with high morbidity and mortality.⁵⁻⁶ The primary aim in treating intertrochanteric fractures in these patients are pain relief, improvement of mobilization, and prevention of complications associated with comorbidities. surgical fixation is the treatment of choice.²⁰⁻²² Because Non operative treatment has got high morbidity and mortality rate. Even with the improvement in implant design, implant choices, and surgical techniques, 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.³⁻⁴ Delayed fracture healing delays the rehabilitation process which in turn influences life quality of the patients. This simultaneously affects the costs burden to both the society and the patients. Hence faster time of union is important for early return of daily activities and reduction of complications. This prospective study demonstrated the fastens the fracture union with Teriparatide 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.¹⁵ In past 20 years, many studies on animals and humans have been done regarding role of Teriparatide in fracture union.^{17,28} 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 30 were females and 10 were males (3:1) which was comparable to other studies on intertrochanteric fractures like Gardenbroek *et al*, Simmermacher *et al* (3.3:1)²⁴⁻²⁵ 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 76 years which was comparable to other studies like Gardenbroek *et al* (79.1 yrs) and Simmermacher *et al* (80.6yrs).²⁴⁻²⁵ 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. Our study included all the 3 types of fractures according to AO classification with majority of patients in A2 group. This trend of maximum patients in

the A2 group is consistent with the international studies like Gardenbroek *et al* and Simmermacher *et al*.²⁴⁻²⁵ This may be attributed 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.²⁶ 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.³⁰ 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*.²⁷ and S.K Singhal *et al*.²³ 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. Likewise, it may prove to be useful in fractures which have a high risk of delayed union or non-union.

CONCLUSION

This study shows faster fracture healing statistically significant in the intertrochanteric fracture patients treated with teriparatide therapy. Faster healing union is vital specially in elderly patients with intertrochanteric fractures to active good functional outcome by reducing morbidity and mortality and this also helps in early return of daily activity, However this necessitate larger studies which can predict efficacy of teriparatide in intertrochanteric fractures.

REFERENCES

1. Brauer CA, Coca-Perraillon M, Cutler DM. Incidence and mortality of hip fractures in the United States. *JAMA*. 2009; 302:1573-9.
2. Shen SH, Huang KC, Tsai YH. Risk analysis for second hip fracture in patients after hip fracture surgery: a nationwide population-based study. *J Am Med Dir Assoc*. 2014; 15:725-31.
3. Frost SA, Nguyen ND, CenterJR, Eisman JA, and Nguyen TV. Excess mortality attributable to hip-fracture: a relative survival analysis. *Bone*. 2013; 56(1):23-9.
4. Wang CB, Lin CFJ, Liang WM. Excess mortality after hip fracture among the elderly in Taiwan: a nationwide population-based cohort study. *Bone*. 2013; 56(1):147-53.
5. Gehrig LMB, Lane JM, O'Connor MI. Osteoporosis: management and treatment strategies for orthopaedic surgeons. *Instruct Course Lect*. 2009; 58:817-32.

6. Schmidt AH, Braman JP, Duwelius PJ, McKee MD. Geriatric trauma: the role of immediate arthroplasty. *J Bone Joint Surg Am.* 2013; 95(24):2030-9.
7. Chiu MH, Hwang HF, Lee HD. Effect of fracture type on health-related quality of life among older women in Taiwan. *Arch Phys Med Rehabil.* 2012; 93: 512–9.
8. Vergara I, Vrotsou K, Orive M. Factors related to functional prognosis in elderly patients after accidental hip fractures: a prospective cohort study. *BMC Geriatr.* 2014; 14: 124–32.
9. Orive M, Aguirre U, García-Gutiérrez S. Changes in health-related quality of life and activities of daily living after hip fracture because of a fall in elderly patients: a prospective cohort study. *Int J Clin Pract.* 2015; 69: 491–500.
10. Koval KJ, Cantu RV. Intertrochanteric fractures. In: Bucholz RW, Heckman JD, Court-Brown CM, editors. *Rockwood and Green's fractures in adults.* 6th Ed. Vol. 2. Philadelphia: Lippincott Williams and Wilkins. 2006:1793–825.
11. Lee PC, Hsieh PH, Chou YC, Wu CC, and Chen WJ. Dynamic hip screws for unstable intertrochanteric fractures in elderly patients—encouraging results with a cement augmentation technique. *J Trauma-Inj Infect Crit Care.* 2010; 68(4):954-64.
12. Gardner MJ, Lorich DG, Lane JM. Osteoporotic femoral neck fractures: management and current controversies. *Instructional Course Lectures.* 2004; 53: 427-39.
13. Eriksen EF, Keaveny TM, Gallagher ER. Literature review: the effects of teriparatide therapy at the hip in patients with osteoporosis. *Bone.* 2014; 67: 246–56.
14. Zhang D, Potty A, Vyas P. The role of recombinant PTH in human fracture healing: a systematic review. *J Orthop Trauma.* 2014; 28: 57–62.
15. Mancilla EE, Brodsky JL, Mehta S. Teriparatide as a systemic treatment for lower extremity nonunion fractures: a case series. *Endocr Pract.* 2015;21:136–42.
16. Borges JL, Freitas A, Bilezikian JP. Accelerated fracture healing with teriparatide. *Arq Bras Endocrinol Metabol.* 2013; 57: 153–6.
17. Aspenberg P, Genant HK, Johansson T. Teriparatide for acceleration of fracture repair in humans: a prospective, randomized, double-blind study of 102 postmenopausal women with distal radial fractures. *J Bone Miner Res.* 2010; 25: 404–14.
18. Bashutski JD, Eber RM, Kinney JS. Teriparatide and osseous regeneration in the oral cavity. *N Engl J Med.* 2010; 363: 2396–405.
19. Lorich DG, Geller DS, Nielson JH. Osteoporotic petrochanteric hip fractures: management and current controversies. *Instructional Course Lectures.* 2004; 53: 441-54.
20. La Valle. Fractures of Hip. In *Campbell's Operative Orthopaedics.* 10th Edition (by Canale ST). Mosby publication. 2003;3:2873-938.
21. Singh CAK, Thong G, Laloo N: Management of Trochanteric Fractures. *Indian J Orthop.* 2006; 40(2):100-2.
22. Oi Brien RM, Shy JC, Bubliss NJ: Internal Fixation of Trochanteric Fractures of the Femur: Report of 103 Consecutive Cases. *J Bone Joint Surg Am.* 1946; 28: 791-7.
23. S.K.Singhal *et al.* Effect of teriparatide in fracture healing of intertrochanteric fracture: A prospective study. 2018; Nov; 4(6)918-923
24. Gardenbroek Tjibbe. J, Segers Michiel JM, Simmermacher RKJ, Hammacher ER. The Proximal Femur Nail Antirotation: An Identifiable Improvement in the Treatment of Unstable Petrochanteric Fractures. *J Trauma.* 2011; 71: 169-74.
25. Simmermacher RKJ, Ljungqvist J, Bail CH *et al.* The new proximal femoral nail antirotation (PFNAW) in daily practice: Result of a multicentre clinical study. *Injury, Int. J. Care Injured.* 2008; 39: 932-9.
26. Huang TW, Yang TY, Huang KC, Peng KT, Lee MS *et al.* Effect of Teriparatide on Unstable Petrochanteric Fractures. *BioMed Res Int.* 2015; 2015: 8.
27. Lou S, Houchen LV, Wang G, Zhang L *et al.* The Effect of Teriparatide on Fracture Healing of Osteoporotic Patients: A Meta-Analysis of Randomized Controlled Trials. *BioMed Res Int.* 2016; 2016:1-10.
28. Yu CT, Wu JK, Chang CC, Chen CL, Wei JC. Early callus formation in human hip fracture treated with internal fixation and teriparatide. *J Rheumatol.* 2008; 35: 2082-3.

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