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ROLE OF TERIPARATIDE THERAPY IN FRACTURE UNION – A PROSPECTIVE STUDY IN INTERTROCHANTERIC FRACTURE CASES

Orthopaedics

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ABSTRACT

Background: Osteoporotic hip fracture is a serious medical problem and a notable burden on the healthcare system.As there is paucity of literature assessing the benefit of Teriparatide in fracture healing, we aim to study whether teriparatide accelerates fracture healing of osteoporotic intertrochanteric femur fractures using a prospective analysis of 2 groups of elderly patients: one that received teriparatide and another received Calcium supplements. **Materials and Methods:** A prospective, randomized controlled study was conducted on Forty patients,with intertrochantric fractures. Two groups (A and B) were made each of twenty patients. Group B patients were given teriparatide injections .For fixation of the fracture and we used proximal femoral nail (PFN) as implant. After the surgery, Group B patients were advised to take daily subcutaneous injections of 20 micro gram teriparatide for 6 months starting from 2nd post op day. Radiographic examinations, including anteroposterior view of pelvis, AP and lateral views of the affected hip at 4 weeks and then monthly were done postoperatively until the fracture united. Radiological assessment was based on the appearance of callus at the fracture site and clinically by assessing functional status by PARKER and PALMER hip mobility score (at 6 months post op).

Result

1. Average union time in patients of GROUP A was 12-16 weeks and GROUP B (45%), it was 8-12 weeks.
2. 70% had no complications related to teriperatide , rest had symptoms of dizziness, joint pain, palpitations.
3. Parker & Palmer Mobility scores at 6 month:-mean mobility score at 6 months in Group A came out 5.5 while in Group B, score was 7.15. The difference of the Parker Mobility score at 6 months was statistically significant. **Conclusion:** Significant faster fracture healing and better functional outcome is seen in patients treated with teriparatide therapy.

KEYWORDS

BACKGROUND

Osteoporotic hip fracture is a serious medical problem and a notable burden on the healthcare system.[1–3] The fracture contributes to high mortality and adverse outcomes in the geriatric population, and the annual number of cases has been estimated worldwide to be as high as 4.6 million by 2025 and 6.26 million by 2050.[4-7] Many patients experience significant functional loss, poor health-related quality of life (HRQoL), and higher mortality rate.[8–10] Faster time of union is important for early return of daily activities and reduction of complications. Surgery is usually indicated, but bringing about pain relief, early weight-bearing, and an early return to the preinjury functional level, which is of critical importance to avoid complications in geriatric patients, remains a challenge for orthopaedic surgeons.[6-7] Osteosynthesis with an extramedullary or intramedullary device is the standard treatment for these fractures[11-12] but fixation stability depends on the quality of bone. Despite achieving perfect reduction and optimal positioning of the implant, failure rate in osteoporotic bone is higher than those in normal bone[13-14] because of age-related decreases in bone regenerative capacity and poor bone stock.[6, 7,.] Recombinant parathyroid hormone (Teriparatide) is the only anabolic medication that has a proven efficacy in stimulating bone formation in addition to promoting growth factors production for fracture healing. Controlled trials have shown that recombinant parathyroid hormone (Teriparatide) can play a valuable role in the treatment of fractures.[6,15-17] In some human trials; it appears to lessen the risk of nonunion[18] and enhance fracture healing.[19-21] Because there is paucity of literature assessing the benefit of teriparatide in fracture healing, we aim to study whether teriparatide accelerates fracture healing of osteoporotic intertrochanteric femur fractures using a prospective analysis of 2 groups of elderly patients: one that received teriparatide and another that received only calcium replacement therapy.

MATERIALAND METHODS

This prospective study was hospital based, and was conducted in the Department of Orthopaedics at RD Gardi Medical College, Ujjain. Patients were selected from those who attended the emergency and outpatient department. A clearance from ethical committee of institute was obtained. Written informed consent was also obtained from all the patients or their family for participation in the study.

Study Population

For this study we recruited 40 patients presented to our hospital with intertrochantric fractures. After enrolment, group assignments were determined by a 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 B patients were given teriparatide injections who were free of severe or chronically disabling conditions other than the intertrochanteric fracture. Participants had to be willing to satisfactorily use a pen-type delivery system or be willing to receive daily subcutaneous injections from a care partner trained to use the injector.

Methodology

On admission to the institution, thorough history about mode of injury, associated injuries, previous medical and surgical history and pretrauma 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-morbity of the patient and routine pre-operative protocol was followed as per our hospital guidelines. Preoperatively, all patients had radiographic examinations including antero- posterior (AP) view of pelvis and AP and lateral views of the affected hip. Fractures were classified according to AO classification for proximal femoral fractures. The exact modality of surgery and type of implant to fix the fracture was planned. Osteosynthesis with intramedullary device was chosen as it is the standard treatment for these fractures in our institute. In our study we used proximal femoral nail (PFN) as intamedullary implant. To minimize drug related variables, patients who were taking antiresorptive drugs prior to fracture were also excluded. Post-operatively, Antibiotics, analgesics and other supportive management were given according to need. A check xray of the operative site was taken to assess proper implant position. Patients were made to sit on bed, do isometric quadriceps & deep breathing exercises from 1st post operative day. Dangling of legs and ROM exercises for knee were taught from 2nd day. Wound inspection was done on 2nd post operative day. The patients were discharged according to the overall well-being of the patient, preferably on third or fourth day, with medications convenient to be taken at home.

Group B patients were advised to take daily subcutaneous injections of 20 micro gram teriparatide for 6 months starting from 2nd post op day.
Follow up:-
Radiographic examinations, including anteroposterior (AP) view of

pelvis, AP and lateral views of the affected hip at 4 weeks and then monthly were done postoperatively until the fracture united. On follow up visits, Patients were evaluated radiologically by assessing appearance of callus at the fracture site and clinically by assessing functional status by PARKER and PALMER hip mobility score[Table1] (at 6 months post op). Primary objective of this study was to compare the effect of once-daily subcutaneous (SC) injection of teriparatide [20 microgram] on radiographic healing in post operative intertrochanteric fractures.

Fracture union is defined as when trabeculae or cortical bone crossing the fracture line in three cortical contacts in radiographs of hip in AP and Lateral views (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 postoperatively.

Our scheduled follow-ups were: At 2 weeks of the surgery (Stitch Removal and clinical assessment) followed by 4,8,12,16, 20, 24 weeks post surgery.

During The Follow Up

The course of fracture healing was documented radiologically (with minimum of 4 weeks between successive radiographs). The moment of complete healing was defined as radiologically complete bone regeneration at the fracture site (atleast 3 cortices should be united).Evaluation of any possible loss of reduction that might have occurred compared to immediate post-operative radiographs. Assesment of functional status by PARKER and PALMER hip mobility scoring at 6 months post op.

RESULTS

We have studied 40 (29female and 11 male) patients of which 20 patients were randomly put in Group A (Control group- given only calcium) and 20 patients were put in Group B (Experiment group- given Teriperatide with calcium). Average age group of the patients was 74years. 20 (12Group A and 8 Group B) patients (60%) had A2 type of fracture pattern. 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 little less, i.e 8-12 weeks. 70% pateints had no complications related to Teriperatide therapy, but a few complications were specifically observed in 30% of experiment group like Dizziness, Cramps, Joint pain, Palpitations. These were not statistically significant. According to Parker & Palmer Mobility scores at 6 month:- mean mobility score at 6 months in Group A came out 5.5 while in Group B, Mobility score was 7.15. The difference between the two groups was statistically significant.

Table I: Parker & Palmer Mobility Score

Mobility	No Difficulty	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

DISCUSSION

Proximal femoral fractures are the frequent injuries affecting elderly patients with osteoporosis and are a burden for the individual, their family, and the health-care system. 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. The primary goals in treating intertrochanteric fractures in these patients are pain relief, improvement of mobilization, and prevention of complications associated with comorbidities. Non operative treatment has little or no role in definitive treatment of these fractures and has high mortality rate ; hence surgical fixation is the treatment of choice.

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.

To date, no systemic treatment is approved for fracture healing. Impaired healing of fractures delays the rehabilitation process, which influences life quality of the patients. At the same time, the associated costs cause an economic burden to both the society and the patients. Faster time of union is important for early return of daily activities and reduction of complications. 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. In past 20 years, many studies on animals and humans have been done regarding role of Teriparatide in fracture union. Only a few studies have been done in India on clinical use of teriparatide in fracture healing, where cost is a major factor. Encouraged with the good results shown in various studies, we have conducted a prospective, randomized controlled, comparative study in 40 post operative patients of intertrochanteric fractures in two groups of 20 each and fracture union time and functional outcome was compared. In our study, we analysed that Teriparatride 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. 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. 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. Furthermore, it can be applied to any types of fractures, including those that will be treated nonsurgically, can be commenced at any time, and can be applied through the entire healing period as well.

CONCLUSION

This prospective randomized controlled study shows statistically significant faster fracture healing and better functional outcome in the intertrochantric fracture patients group treated with teriparatide therapy. The faster union may be 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.

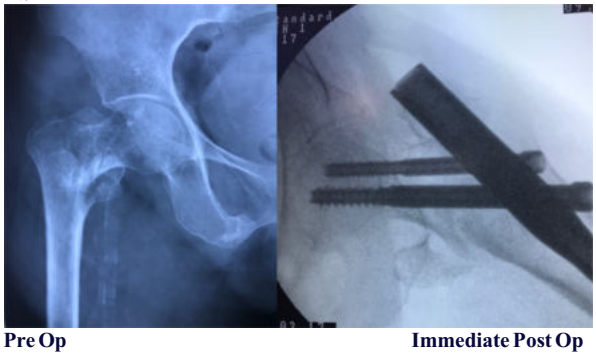
ILLUSTRATTIONS:-

Pt.1

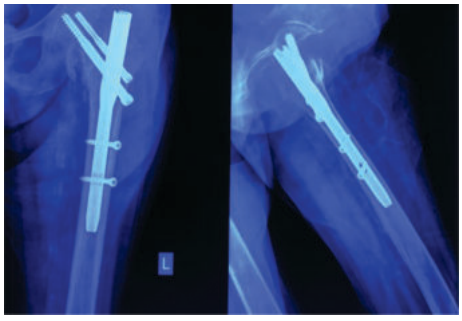
Pre Op **Immediate Post Op**

Post Op 8 Weeks **Post Op 12 Weeks (Fracture United)**

Pt. -2



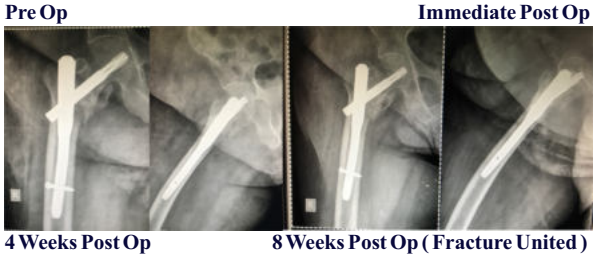
Pre Op **Immediate Post Op**



Fracture United In 8 Weeks

Pt. 3

Pre Op **Immediate Post Op**



4 Weeks Post Op **8 Weeks Post Op (Fracture United)**

Pt.-4

Pre Op **Immediate Post Op**

4 Weeks Post Op **10 Weeks Post Op (Fracture United)**

Pt. HS 82/M

Pre Op **Immediate Post Op**

4 Weeks Post Op **16 Weeks Post Op (Fracture United)**

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