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To study the role of short term teriparatide injection in the management of intertrochanteric fracture of hip in elderly patients after osteosynthesis

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Abstract
Introduction: Osteoporosis negatively affects the patients quality of life and results in high Healthcare cost. Teriparatide is a synthetic polypeptide hormone that contains 1-34 amino acid fragment of the recombinant human parathyroid hormone and it is claimed to fasten fracture healing. Hence we decided to carry out a study to find out the effect of teriparatide injection if given for short term, in elderly osteoporotic intertrochanteric fractures, in the postoperative period.
Materials and Methods: We carried out non randomised, controlled non inferiority clinical trial at MIMER medical college talegaon dabhade from 1st august 2018 to 31st July 2019. We enrolled patients into two groups. Group A received injection teriparatide 20 microgram daily with 400 IU of Vitamin D3 and 1200 milligram calcium for 3 months in the post-operative period. Group B received only 400 IU of Vitamin D3 and 1200 milligram of calcium for 3 months. We followed up patients at 6 weeks, 12 weeks, 24 weeks, 36 weeks for pain at fracture site, radiological sign of union.
Results: Results of our study showed that Union time in group A(patients who received teriparatide) was significantly less than group B. Harris hip score was also significantly better in group A as compared to group B.
Conclusion: In this prospective, non randomised controlled, non-inferiority clinical trial 3 months of injection teriparatide after surgery was associated with significantly shorter time for fracture union, better functional outcome and no complications.

Keywords: Teriparatide, intertrochanteric, fracture, short duration, union, type

Introduction
In osteoporosis bone density decreases and fractures are most likely, especially in the Hip, spine and wrist, more likely after menopause in females or in those persons like smokers or malnourished and ill people [1 2]. Special x-ray based scan like DEXA is used for diagnosis, though simple x-ray can be suggestive of diagnosis [3]. Treatment consists of drugs to prevent bone loss further, along with exercise and dietary adjustment with extra intake of magnesium, calcium and Vitamin D etc [3]. Among drugs most popular ones are bisphosphonates (Antiresorptive), oestrogen agonist or antagonist (SERMS), calcitonin, monoclonal antibodies (Denosumab), parathyroid hormone (Teriparatide) etc [3].
Osteoporosis negatively affects the patients' quality of life and results in high Healthcare cost [4]. In an operated case if one more surgery is required to stabilize the osteoporotic fracture then cost increases further (Example: Implant cut out in intertrochanteric fractures of hip) [4]. Teriparatide is a synthetic polypeptide hormone that contains 1-34 amino acid fragment of the recombinant human parathyroid hormone [5]. It's mechanism of action is stimulation of formation by activation of osteoblasts more than osteoclasts (By intermittent exposure). Firstly it stimulates active remodelling sites like fracture and secondly, it also increases new remodelling sites in previously inactive osteoporotic bone [6]. Beneficial effect of teriparatide in osteoporotic spine fractures has been proved beyond doubt in many studies but it's beneficial effect in osteoporotic hip fracture is somewhat controversial [7].
Hence we decided to carry out a study to find out the effect of teriparatide injection if given for short term, in elderly osteoporotic intertrochanteric fractures, in the postoperative period.

We aimed to study short term, basically to take advantage of active remodelling sites of fracture, which can help reduce the cost of therapy of this costly drug instead of long term study.

Materials and Methods

We carried out non randomised, controlled non inferiority clinical trial at MIMER Medical College Talegaon Dabhade from 1st august 2018 to 31st July 2019. We obtained local ethical committee approval. Our sample size was 20 (10 in each group). Selection of cases in each group was done after matching of inter trochanteric fracture type by Jensen's modification of Evans classification (3 types i.e.2 part, 3 part and 4 part fractures), in patients above 65 years in whom intertrochanteric femur fracture was fixed by dynamic hip screw and plate. We excluded patients with other associated fractures, patient with history of treatment for malignancy, pathological fractures, non- osteoporotic fractures, compound fractures, hypercalcemia and hypoparathyroidism in addition to patients receiving other medication for osteoporosis except Calcium and Vitamin D. We took written and informed consent from patients. We enrolled patients into two groups. Group A received injection teriparatide 20 microgram daily with 400 IU of Vitamin D3 and 1200 milligram calcium for 3 months. Group B received only 400 IU of Vitamin D3 and 1200 milligram of calcium for 3 months. We used Singh's index for osteoporosis on X-Ray pelvis with both hip joints and chose grade 3 or below as a definite indicator of osteoporosis. We did not use DEXA as it was very difficult to use in fracture setting and DEXA machine was not available in our Institute. We followed up patients at 6 weeks, 12 weeks, 24 weeks, 36 weeks for pain at fracture site, radiological sign of union (3 cortex bridging and callus), side effects (like nausea, headache, dizziness and hypercalcemia) and final evaluation by Harris hip score. Patients were operated by DHS and plate once they became fit. In the postoperative period there was started on injection teriparatide after 48 hours postop. They were given IV antibiotics and analgesics as need. Physiotherapy was started as early as possible. Full weight bearing was deferred till signs of union were visible on follow up visits.

Results

Table 1: Important data of groups

	Group A	Group B	P value
Male	6F & 4M	7F & 3M	>0.05
Age(yrs)	73.0	70.48	>0.419
Duration of hospital stay (Days)	8+/- 1	8+/- 1	0.85
Union time	10.6weeks	13.6 weeks	<0.001
Haris Hip score	71.41	78.01	<0.05
Avg time for surgery (min)	131.6 +/- 30.4	119.0+/- 40.6	P=0.221
Implant cutout and malunion	0	1	p>0.05

Distribution of patients according to Jensen's classification
3 Patients of Jensen's modification of Evan's classification Type1.
4 patients of type 2.
3 patients of type 3.
Mann Whitney Parametric test was used for data analysis

Discussion

Osteoporotic fractures are difficult to treat only by fixation of fractures and Calcium and Vitamin D supplementation. Intertrochanteric hip fractures are leading cause of morbidity and mortality in osteoporotic patients [7]. In a trial to assess the effects of teriparatide therapy at the hip in patients with osteoporosis by Erikson E F *et al*, encouraging results were obtained with teriparatide injection [7]. Recently there are many case reports and clinical trials which claim that fracture healing is accelerated by injection teriparatide which is an osteoanabolic agent [8, 9]. A prospective randomised controlled trial by Aspenberg P et- al shows that distal radial fracture heals faster when given injection Teriparatide as compared to placebo [10]. However there are limited such trials about osteoporotic intertrochanteric fractures till today. Teriparatide injection is a costly drug for inter trochanteric fracture patients as it increases the cost of treatment if given for prolonged period as recommended by numerous authors and can rarely induce osteosarcoma. However, if given for short period of time, in the postoperative period when fracture healing has already begun (Active remodelling site with plenty of osteoblasts), we can hasten the healing of fracture according to published literature [11, 12].

We wanted to exploit this benefit of teriparatide. Results of our study showed that Union time in group A (Patients who received teriparatide) was significantly less than group B. Harris hip score was also significantly better in group A as compared to group B. There was no significant difference between two groups as regards to age, sex, duration of hospital stay, average time for surgery or non-union. However in one patient in group B there was implant cut out and revision surgery with PFN A2 was done, which united later. This could be due to poor bone stock and varus collapse of proximal fragment due to osteoporosis [13]. In our study no significant side effects of teriparatide occurred like osteosarcoma or even significant gastrointestinal upset [14]. We had already excluded many confounding factors earlier and matched the groups. However there were many limitations of our study such as small sample size, non-randomised trial, nonuse of DEXA scan (Singh's index was used) and nor did we do any vitamin D level at the baseline or at the end of treatment.

Conclusion

In this prospective, non-randomised controlled, non-inferiority clinical trial 3 months of injection teriparatide after surgery was associated with significantly shorter time for fracture union, better functional outcome and no complications. However a prospective, randomised controlled study will be necessary before coming to final conclusion.

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