



## EVALUATION OF THE OUTCOME OF THE TERIPARATIDE INJECTION IN ACHIEVING EARLY CLINICAL AND RADIOLOGICAL UNION IN POST-OPERATED CASES OF INTERTROCHANTERIC FRACTURE OF FEMUR – A PROSPECTIVE COMPARATIVE OBSERVATIONAL STUDY

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### ABSTRACT

**Introduction:** Globally, intertrochanteric fractures of the femur have shown an increasing incidence amongst the fractures around the hip over the past few decades. With multitude of management options aiming at early union, good early functional outcome and prevention of further fragility fractures, it becomes essential to evaluate and formulate a standard treatment protocol for them. The aim of this study is to evaluate the clinical and radiological union outcomes of administration of Teriparatide to operated patients of Intertrochanteric fracture femur starting from early post-operative period. **Material and Methods:** A prospective comparative observational study among 70 patients over a period of 2 years from 2020-22. Plain radiography to determine fracture healing and VAS, HHS to determine functional outcome were used. Data was tabulated analysed using Microsoft excel and SPSS version 21. Chi-square test and unpaired t test were used to find the association and mean differences between two groups. A p-value of less than 0.05 was considered statistically significant. **Results:** Age of the participants ranges from 60 – 82 years with mean (SD) age 71.2 (6.9) years. Out of 70 patients, 40 (57%) patients were females and 30 (43%) were males. The mean (SD) time taken to union of bones at fracture site in Group I (Injection Teriparatide plus Calcium Supplements) was significantly lower than Group II (Calcium Supplements only). The mean (SD) Visual Analogue Scale (VAS) and Harris Hip Score (HHS) also found significantly lower in Group I as compared to Group II **Conclusion:** We concluded that, present study found a significant reduction of time taken to union in elderly patients with intertrochanteric femur fractures who were provided Teriparatide treatment as compared to other group of patients. Also shown improvement in the functional outcomes (low VAS, high HHS scores) in patients provided Teriparatide treatment as compared to other group.

### KEYWORDS : Teriparatide, Intertrochanteric, Fracture, Post-Operative

#### Introduction:

Globally, intertrochanteric fractures of the femur have shown an increasing incidence amongst the fractures around the hip over the past few decades and are associated with increased incidence of morbidity and mortality of the patients and with increasing economic burden. 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 –(Cooper et al., 1992; Gullberg et al., 1997; Mir & Haidukewych, 2022).

Ageing continues to be one of the main risk factors for fractures, and osteoporosis is a disease that is most prevalent in older adults, even though there is significant variation in fracture incidence worldwide and fracture risk in various geography, ethnicity, and socioeconomic status. Fragility fractures are extremely rare before the age of 50, and after that point, their frequency rises steadily as people age. These fractures, which are most frequently fragility fractures brought on by osteoporosis and are frequently seen in the elderly population. When these intertrochanteric fractures appear in young people, high-energy trauma is the cause(Bouvard et al., n.d.).

Numerous risk factors, both reversible and irreversible, are linked to osteoporosis. The most significant ones include the world's population's tendency to live longer, nutritional factors like vitamin D deficiency and undernutrition, drugs, postmenopausal osteoporosis, alcohol consumption, level of activity, and comorbidities like renal failure –(Uriz-Otano et al., 2016).

Fragility fractures are linked to severe disability, significant morbidity, a decrease in quality of life, and functional limitations in addition to the inherent difficulties associated with fixation that may result in fixation failure. Therefore, it becomes crucial to treat osteoporosis in addition to fixing the fracture in order to achieve early union, a positive functional outcome, and the prevention of future fragility fractures ""(Oostwaard, 2018).

Apart from fracture fixation, osteoporotic fracture management calls for ancillary treatments such as calcium and vitamin D3, anti-resorptive drugs like bisphosphonates, denosumab, and hormone replacement therapy, and anabolic agents such as Teriparatide (Bouvard et al., n.d.; Reid et al., n.d.). Teriparatide, a recombinant 1-34 fragment of human parathyroid hormone (PTH), stimulates the growth and activity of osteoblasts, the cells in charge of forming bones, leading to increases in bone tissue. Direct stimulation of bone formation, as opposed to antiresorptive drugs, may not only improve bone strength but also speed up the healing of fractures (Gehrig et al., 2009). Teriparatide showed promise as an attractive agent to promote fracture healing and reduce the risk of non-union –(Canintika & Dilogo, 2020). Teriparatide appears to hasten bone healing and enhance functional recovery following fracture at various skeletal sites, according to several published literature and systematic reviews –(Canintika & Dilogo, 2020; Han et al., 2020; Huang, Chuang, et al., 2016; Huang, Huang, et al., 2016; Kim et al., 2017).

With multitude of management options aiming at early union, good early functional outcome and prevention of further fragility fractures, it becomes essential to evaluate and formulate a standard treatment protocol for them. The purpose of this study is to evaluate the clinical and radiological union outcomes of administration of Teriparatide to operated patients of Intertrochanteric fracture femur starting from early post-operative period.

#### Materials and Methods:

A Prospective Comparative Observational Study was conducted among 70 (35 in each group) post-operative patients with intertrochanteric fracture of femur in a tertiary care hospital in Western Maharashtra during the period of 2 years from 2020 to 2022.

All the post-operative patients for intertrochanteric fracture of femur with age more than 60 years were included in the study. Patients who

were unwilling, previously treated with PTH and patients with unstable pattern of Intertrochanteric fracture / Traumatic Intertrochanteric fracture, concomitant mental instability and known malignancy within 5 years before surgery were excluded from study.

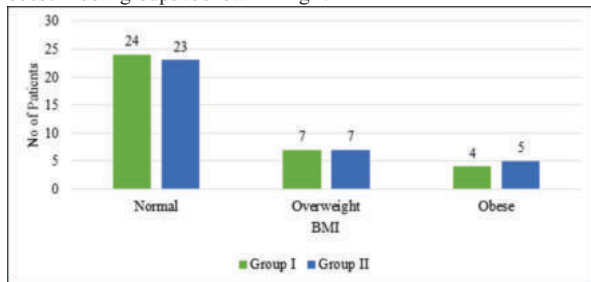
Patients were assigned to respective groups by alternatively one to first group followed by second group and vice versa. Patients' clinical data were obtained from their records. In addition, specific information regarding the fracture classification by and immediate or early post-operative complications were documented. Patients in Group I managed primarily with Injection Teriparatide (Self-administered dose of 20µg subcutaneously, daily for 18 months) along with Calcium Supplements and Group II patients managed with Calcium Supplements only.

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. 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. Assessment of functional status was done by Pain Score using Visual Analogue Scale (VAS) and Harris Hip Score at one (01), three (03) and six (06) months post op and assessment and analysis of any complications were observed.

Data was tabulated and analysed using MS Excel and SPSS 21 version. Discrete variables were summarized as proportion and continuous variables as means ± standard deviation. Bivariate analysis was done using Chi-square test to determine the association between both groups. Functional and radiographic results were compared between the two groups with the unpaired *t*-test. A *p*-value of less than 0.05 was considered statistically significant. Study was approved by Institutional ethics committee. WHO informed consent form and participant information sheet was used for verbal consent.

**Results:**

Age of the participants ranges from 60 – 82 years with mean (SD) age 71.2 (6.9) years. Out of 70 patients, 40 (57%) patients were females and 30 (43%) were males. The mean (SD) height, weight and BMI (Body Mass Index) was 171.2 (7.7) cm, 68.9 (10.9) kgs and 23.7 (4.6) kg/m<sup>2</sup> respectively as shown in Table 1. A few patients were found obese in both groups as shown in Fig 1.



**Figure 1. Distribution of BMI among Groups (p = 0.936)**

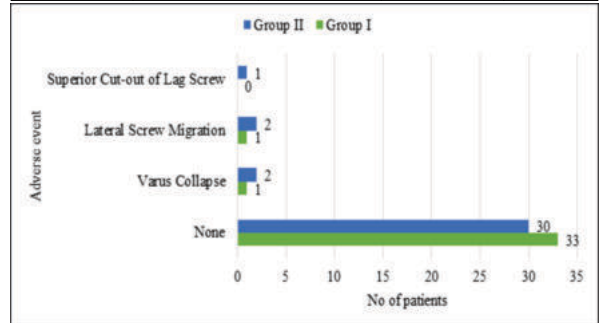
**Table 1. Comparison of general characteristics of patients**

Characteristics		Group I (35)	Group II (35)	Total (70)	p value
Age (years)	Mean (SD)	71.0 (7.2)	71.3 (6.8)	71.2 (6.9)	0.838
Gender (N, %)	Male	17 (24.3)	13 (18.6)	30 (42.9)	0.334
	Female	18 (25.7)	22 (31.4)	40 (57.1)	
Height	Mean (SD)	170.4 (8.2)	171.9 (7.1)	171.2 (7.7)	0.412
Weight	Mean (SD)	69.3 (10.8)	68.6 (11.1)	68.9 (10.9)	0.811
BMI		23.9 (4.2)	23.5 (4.9)	23.7 (4.6)	0.646

The mean (SD) time taken to union of bones at fracture site in Group I (Injection Teriparatide plus Calcium Supplements) was significantly lower than Group II (Calcium Supplements only). The mean (SD) Visual Analogue Scale (VAS) and Harris Hip Score (HHS) also found significantly lower in Group I as compared to Group II as shown in Table 2. The adverse events in Group I was 5.7% (2 out of 35), whereas in Group II it was more than double (5, 14.3%) as shown in figure 2.

**Table 2. Comparison of clinical and radiological union outcomes**

Outcome	Group I (35)	Group II (35)	p value	
Time taken to Unite	149.9 (47.7)	187.9 (80.4)	0.020*	
VAS	1 <sup>st</sup> month	61.1 (8.5)	65.7 (10.9)	0.053
	3 <sup>rd</sup> month	47.7 (9.5)	50.5 (10.0)	
	6 <sup>th</sup> month	32.7 (8.6)	38.3 (6.9)	
HHS	1 <sup>st</sup> month	35 (6.4)	37.6 (6.6)	0.102
	3 <sup>rd</sup> month	56.4 (6.3)	61.5 (5.2)	
	6 <sup>th</sup> month	71.7 (6.1)	79.5 (3.4)	



**Figure 2. Comparison of adverse events among both groups**

**Discussion:**

Since osteoporotic hip fracture is a serious medical problem and a notable burden on the healthcare system, there is a medical need for therapies that improve hip fracture healing. Recently, there has been heightened interest in using osteoanabolic agents for osteoporosis treatment. The aim of this study was to evaluate whether the administration of daily Teriparatide could improve early postoperative outcomes in hip fractures.

Huang et al reported that Teriparatide yields better clinical outcomes of unstable per trochanteric fractures in 44 patients who underwent DHS fixation at 3 and 6 months postoperatively (Huang, Chuang, et al., 2016). Tu et al demonstrated that Teriparatide therapy significantly decreased visual analogue scale pain scores, increased functional scores but suggested that therapy should continue for at least six months to ensure it is effective (Tu et al., n.d.). However, because PTH treatment is more expensive than other medical treatments for osteoporosis and uncomfortable subcutaneous injection remains the only licensed route of administration, (Morley, 2005) the greatest challenge of delivering this study was that of identifying a sufficient number of eligible patients. For these reasons, we couldn't recommend the use of expensive injection therapy for patients over three months. The dose, duration and cost effectiveness of treatment remain in question (Moon et al., 2012). Nevertheless, in the present study, significant differences between groups regarding the functional endpoints were observed. Two months of Teriparatide use after surgery improved functional score and decreased pain compared with conventional treatment. This earlier recovery of function might possibly reflect an earlier mature fracture union due to Teriparatide.

Despite of the difficulties that are present in monitoring the healing process in human, the effects of PTH on normal primary fracture have been investigated (Aspenberg et al., n.d.; Peichl et al., n.d.; Pietrogrande et al., n.d.). Peichl et al reported in a prospective, randomized, controlled study of 65 patients and concluded that PTH 1–84 accelerates fracture-healing in pelvic fractures and improves functional outcome in elderly patients with osteoporosis (Peichl et al., n.d.). Moon et al demonstrated that two-month Teriparatide treatment is considered to be useful to relieve pain rapidly, to allow walk in early stage, and to reduce side effects caused by drug administration in pelvic insufficiency fracture patients with osteoporosis (Moon et al., 2012).

Recently, Huang et demonstrated that postoperative use of Teriparatide for 6 months appears to be an effective adjunct therapy in the treatment of patients who underwent surgery using a DHS for osteoporotic intertrochanteric fractures (Huang, Chuang, et al., 2016). In our study, we confirmed that radiographic outcomes of intertrochanteric hip fractures were improved in the group treated with daily Teriparatide.

Shortening or varus collapse are common postoperative complications in unstable three- and four-part intertrochanteric fractures because of

pronounced impaction of the fracture. Cement-augmentation has been widely used for osteoporotic intertrochanteric fractures, it has its own set of failure modes and makes subsequent revision surgeries more complex and technically demanding. On the other hand, significant reduction of sliding of lag screw, femoral shortening, varus collapse, and incidence of cut-out of the lag screw has been reported in patients who received Teriparatide (Lee et al., 2010; Mattsson et al., 2005). Similarly, in the present study, there was a few adverse events in cases treated with Teriparatide as compared to other.

Because slow recovery after hip fracture has been associated with negative consequences and complications, if a pharmacological therapy could improve hip fracture healing, this may reduce the number of revision surgical procedures and potentially improve other aspects important for recovery, such as early ambulation and rapid return to function. We believe that even a slight improvement in union time is important for elderly populations with unstable per trochanteric fractures, allowing them to return to daily activities sooner and reducing overall morbidity (such as pneumonia and pressure ulcer) and mortality.

The present study had some limitations. Since this was a prospective observational study with all the inherent weaknesses and selection biases, the conclusions from the results are limited. Other limitations were the sample size and the patient allocation process. In order to address these limitations, strict inclusion and exclusion criteria were applied, and we used objective data such as digitized plain radiographs which allowed us to achieve excellent reproducibility, and compared postoperative complication rates.

We concluded that, present study found a significant reduction of time taken to union in elderly patients with intertrochanteric femur fractures who were provided Teriparatide treatment as compared to other group of patients. Also shown improvement in the functional outcomes (low VAS, High HHS scores) in patients provided Teriparatide treatment as compared to other group. Further clinical trials at large-scale are warranted to determine significantly superior clinical outcomes.

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