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ROLE OF SUPPLEMENTAL TERIPARATIDE THERAPY TO AUGMENT FRACTURE HEALING IN INTERTROCHANTERIC FRACTURES OF THE HIP IN ELDERLY PATIENTS

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Abstract

Background: Osteoporotic intertrochanteric femur fractures remain a significant challenge for orthopedic surgeons, despite advancements in surgical techniques. The compromised bone quality inherent to osteoporosis often makes achieving stable fixation and favorable outcomes difficult. Consequently, contemporary research has shifted towards a more holistic management strategy—integrating surgical intervention with targeted treatment of the underlying osteoporosis. This comprehensive approach aims to improve long-term outcomes, reduce complication rates, and enhance quality of life in this vulnerable patient population. Teriparatide, a recombinant form of human parathyroid hormone, is increasingly recognized as a potential therapeutic agent for enhancing fracture healing, with supportive evidence from both animal models and clinical studies. The present study investigates the role of teriparatide therapy in promoting fracture healing in patients with osteoporotic intertrochanteric femur fractures treated surgically. By evaluating its effects on both bone union and functional recovery, this work aims to provide evidence that could inform future research and support the development of improved treatment strategies for these challenging injuries.

Methods: In this study, osteoporotic patients who underwent surgical fixation for intertrochanteric femur fractures were monitored postoperatively. Participants were divided into two groups: one received adjunctive teriparatide therapy, while the other was provided with supplemental calcium and vitamin D. The objective was to evaluate the influence of teriparatide on fracture union time, bone mineral density (BMD), and the incidence of postoperative fracture-related complications. Functional outcomes were measured using the Harris Hip Score.

Results:A higher proportion of female patients was noted in the study cohort. All 30 participants achieved fracture union within 24 weeks. At the 6-week follow-up, no evidence of union was detected in either group. By 12 weeks, the control group (Group A) demonstrated a union rate of 13.33% (two patients), whereas the teriparatide group (Group B) achieved a union rate of 56.25% (nine patients). This difference was statistically significant ($p=0.01$), indicating that teriparatide may substantially accelerate fracture healing in osteoporotic intertrochanteric femur fractures. A decrease in tip–apex distance (TAD) reflected progressive migration of the helical blade as weight-bearing commenced. For the first 12 weeks, TAD values were comparable between groups. By 24 weeks, however, the mean TAD in Group A was 22.57 ± 1.33 mm, significantly lower than the 24.26 ± 1.92 mm observed in Group B ($p=0.031$). These findings suggest that earlier bone union and consolidation in the teriparatide group helped limit blade migration, thereby reducing the likelihood of screw cutout, hip pain, and implant failure.

Conclusions: In conclusion, the findings of this study indicate that teriparatide enhances fracture healing and promotes improvement in bone mineral density in patients with osteoporotic intertrochanteric hip fractures. Although its use is associated with higher treatment costs, the added benefits—such as earlier fracture union, notable gains in bone density and mass, and superior functional recovery—justify the investment. These results position teriparatide as a valuable adjunct

in the management of osteoporotic hip fractures, with the potential to deliver better long-term patient outcomes.

Keywords: Intertrochanteric fracture, Teriparatide, helical blade

INTRODUCTION:

Osteoporotic fractures are linked to severe pain, elevated rates of morbidity and mortality, and a marked reduction in quality of life. Beyond their impact on patients' physical health, these injuries also place a substantial economic burden on healthcare systems, driven by the extensive requirements for treatment, rehabilitation, and prolonged care. [1]. Projections indicate that by 2040, the global population at high risk for osteoporotic fractures will surpass 300 million. This concerning trend underscores the escalating societal burden of the disease and its far-reaching impact on healthcare systems across the world [2].

In the year 2000 alone, approximately nine million new osteoporotic fractures occurred worldwide, reflecting the extensive global impact of the condition. [3]. With the aging of the global population—especially among individuals aged 65 years and above—the incidence of hip fractures alone is projected to reach approximately 6.26 million cases by 2050. [4].

Although the incidence of osteoporotic fractures—such as hip, vertebral, and non-vertebral—differs considerably across regions, the disease burden is steadily increasing in Asia, Latin America, and the Middle East. [5,6,7]. According to projections by Cooper et al., by 2050, Asia alone is expected to represent about 51% of all hip fractures in women aged 65 years and older. When combined with Latin America and the Middle East, these regions are anticipated to account for nearly 70% of global hip fractures in this demographic. [4]. The prevalence of vertebral fractures shows considerable regional variation. Among women over the age of 50, reported rates range from 11% to 19% in Latin American countries, 5% to 30% in Asian countries, and 20% to 46% in Middle Eastern countries. [8].

Osteoporosis management aims to either suppress bone resorption or promote bone formation. Agents such as bisphosphonates, denosumab, estrogen receptor modulators, and estrogens act primarily by reducing bone resorption, whereas romosozumab has a dual effect—both decreasing resorption and enhancing formation. Teriparatide, the first approved anabolic therapy for osteoporosis, is a recombinant form of human parathyroid hormone ([PTH] 1–34) that improves bone mass and quality by stimulating osteoblast activity. [9, 10]. Teriparatide enhances bone microarchitecture by promoting the formation of both trabecular and cortical bone, thereby counteracting the structural deterioration associated with osteoporosis. [11].

Randomized controlled trials (RCTs) have confirmed the efficacy and safety of teriparatide, demonstrating that its use is associated with a reduced fracture risk compared with placebo, alendronate, or risedronate. [9, 12, 13]. Of note, Findings from the Fracture Prevention Trial indicate that extended use of teriparatide is linked to a lower incidence of non-vertebral fractures and a reduction in back pain.[14, 15].

Consistent with findings from RCTs, multiple observational studies conducted in the United States, Europe, and Japan have also reported the effectiveness of teriparatide. [16, 17]. The Direct Assessment of Non-vertebral Fractures in Community Experience (DANCE) study conducted in the USA found a 43% reduction in non-vertebral fracture incidence during the final six months of teriparatide therapy (months 18–24) compared with the initial six months. Notably, this decline was sustained throughout the 24-month follow-up period after treatment cessation.

[18]. Similarly, the European Forsteo Observational Study (EFOS) and the Extended Forsteo Observational Study (ExFOS) reported reductions in the odds of clinical fractures by 39% and 47%, respectively, during the 12–18 month period compared with the first six months of treatment. [19, 20]. In addition, the Japan Fracture Observational Study (JFOS) demonstrated a 59% reduction in the risk of clinical fractures during the final six months of teriparatide therapy (months 18–24) compared with the initial six months in Japanese patients.

[21]. Furthermore, An integrated analysis of these four studies revealed a reduction in hip fracture rates during periods beyond six months of teriparatide therapy compared with the initial six-month period. [16, 17]. Across all four observational studies, teriparatide treatment was associated with reduced back pain and improved quality of life in patients. [18,19,20,21,22].

Collectively, these studies demonstrate an association between teriparatide use and reduced fracture risk, along with decreased back pain, in populations from the USA, Europe, and Japan. However, robust large-scale data on its effectiveness, as well as on treatment persistence and adherence in real-world clinical settings across Asia, Latin America, and the Middle East, remain limited. These regions differ in several ways from the previously studied populations in the USA and Europe. In the countries participating in the Asian and Latin America Fracture Observational Study (ALAFOS), factors such as a rapidly aging population, a rising prevalence of osteoporosis, a high proportion of treatment-naïve patients, and variability in clinical practices and osteoporosis management guidelines are notable. [23,24,25,26]. Additionally, Calcium intake in Asia–Pacific and South American

populations is generally lower than that of Western populations. In many South, East, and Southeast Asian countries, daily calcium consumption is below 400 mg, whereas South American countries typically report moderately low intakes, ranging from 400 to 700 mg per day.
[27].
The lack of evidence on teriparatide's effectiveness in Asia, Latin America, and the Middle East—coupled with projections of a rising burden of osteoporotic fractures in these regions over the coming three decades [28] highlights the necessity of investigating the effectiveness of osteoporosis drug treatments in a real-world setting in these geographies.

MATERIALS AND METHODS

After obtaining the necessary institutional ethical clearance, a prospective randomized controlled study was conducted at SAVEETHA Hospital, Thandalam, Chennai, between September 2023 and February 2024. The study included patients over the age of 50 years presenting with isolated unilateral intertrochanteric femur fractures and established osteoporosis confirmed by dual-energy X-ray absorptiometry (DEXA) scan. A T-score of –2.5 or lower was considered diagnostic of osteoporosis and served as an inclusion criterion.
The surgical protocol and choice of implant were standardized for all cases, consisting of closed intramedullary fixation with a proximal femoral nail (single helical blade, titanium, from a single manufacturer). All procedures were performed by the same team of surgeons to minimize inter-operator variability. Routine blood investigations were carried out to exclude other metabolic conditions that could potentially influence outcomes; patients with such conditions were excluded from the study.
Exclusion criteria were as follows: (1) patients unwilling to provide consent; (2) known allergy to teriparatide or a documented history of drug hypersensitivity; (3) prior use of teriparatide or other antiresorptive agents; (4) severe comorbidities associated with poor life expectancy; (5) presence of other metabolic bone disorders; (6) a DEXA T-score greater than –2.5 at presentation; and (7) multiple fractures.
All procedures adhered strictly to ethical guidelines, and written informed consent was obtained from all participants. A detailed history, along with general physical and systemic examination, was recorded, followed by relevant laboratory and imaging investigations. Patients with a body mass index (BMI) below 18.5 kg/m² were excluded, as inadequate nutrition could confound fracture healing outcomes. Eligible patients were counseled regarding the surgical procedure, postoperative rehabilitation, and the administration of teriparatide in addition to standard osteoporosis therapy. The potential benefits and adverse effects of teriparatide were explained, and consent for its use was obtained prior to enrollment.
. Patients who opted out of receiving additional teriparatide were placed in Group A, while those who agreed to the therapy were assigned to Group B. The two groups were kept entirely separate, with no sharing of treatment details, medical records, or demographic information. Daily monitoring of patient progress was carried out by nurses and paramedics who were unaware of the study's specifics, alongside the surgical team.
Group A was given calcium and vitamin D3 supplements along with the standard postoperative medications, which included antibiotics, pain relievers, and proton pump inhibitors. Group B received a daily subcutaneous injection of 20 micrograms of teriparatide into the anterolateral thigh starting from the fifth day after surgery, in addition to the same calcium, vitamin D3, and standard postoperative care provided to Group A.
The same brands of calcium, vitamin D3, and other medications were administered to both groups. In group B, all patients received the identical brand of teriparatide injection. Both groups were carefully monitored for any drug-related side effects, with particular attention to group B, including injection site reactions, muscle cramps, and behavioral changes.
Additional blood tests performed included serum parathyroid hormone (PTH), serum calcium (Ca^{2+}), serum phosphate, and serum vitamin D levels. PTH levels were assessed using the serum electrochemiluminescence immunoassay (ECLIA) method, with a biological reference range of 15–65 pg/ml.
. The collected data were recorded using a specially designed form. The study incorporated the Boyd and Griffith classification of intertrochanteric (IT) fractures. Patients who met the eligibility criteria and passed the preanesthetic evaluation were scheduled for surgery and treated with proximal femoral nailing. Radiographic examinations were performed for all patients, including anteroposterior (AP) views of the pelvis with both hips, as well as AP and lateral views of the affected hip with zero magnification, taken preoperatively, on postoperative day 2, and then at 6, 12, and 24 weeks.
During surgery, the quality of fracture reduction was evaluated fluoroscopically and deemed acceptable if the fracture gap measured less than 5 mm, with varus-valgus angulation under 10°, and/or anteversion-retroversion less than 10°. The helical blade was considered ideally positioned if located in the central-central quadrant on both AP and lateral views. Placement in the inferior-central or central-posterior quadrants was also acceptable.
Postoperative zero magnification AP and lateral X-rays were taken on day 2, and measurements of the neck-shaft angle, tip-apex distance, and femoral neck length were conducted using a simple novel method.

Following surgery, doctors monitored the patient's recovery by using serial X-rays. They checked for movement of the surgical blade, a process referred to as **blade migration**, by measuring its tip apex distance. They also assessed for **varus collapse**, a type of bone collapse, by observing changes in the neck and shaft angles of the bone.

The patient's physical rehabilitation began on the second day after the operation with quadriceps and knee bending exercises. About three weeks later, they were advised to begin **toe touch weight bearing** with a walker. Full weight-bearing, still with the assistance of a walker, was permitted after six weeks. Most patients were able to walk without any assistance approximately 10 weeks post-surgery.

. Patients received clinical follow-up evaluations at 6, 12, and 24 weeks. These evaluations included a **blood investigation**, a **DEXA scan**, an **X-ray**, and a **clinical examination**.

Fracture healing, or **radiographic union**, was determined by specific signs on the X-rays, such as the presence of a bridging **callus**, the restoration of **trabeculae**, the continuity of the **cortex**, and the disappearance of the fracture line. This union was formally assessed using the **Radiographic Union Score of Hip (RUSH)** score, which was recorded

Patients were brought back for follow-up visits at 6, 12, and 24 weeks. During these appointments, doctors performed a **clinical examination**, took **blood samples**, and conducted **DEXA scans** and **X-rays**.

The primary goal was to check for **radiographic union**, which is the term for a healed fracture. This was determined by looking for four specific signs on the X-rays: new bone formation that bridges the fracture site (bridging **callus**), the restoration of the inner bone structure (**trabeculae**), a continuous outer bone layer (**cortical continuity**), and the disappearance of the original **fracture line**. The healing process was formally graded using a tool called the **Radiographic Union Score of Hip (RUSH)** score.

[20].Functional outcome of the patients was obtained using the Harrison Hip Score (HHS) [21]. The study's data, collected from a total of 30 patients—15 in the **non-teriparatide** group and 15 in the **teriparatide** group—was organized in a master chart. A biostatistician then performed a statistical analysis on this data using **Microsoft Excel** (2019 version). They used an **unpaired t-test** to compare the two groups, and a **p-value** of less than 0.05 was set as the threshold for statistical significance. The variation within the data was reported as the **standard deviation (SD)**.

DISCUSSION

steoporosis is characterized by a reduction in bone mass and deterioration of bone microarchitecture, resulting in increased fragility and susceptibility to fractures. These fragility fractures often lead to significant pain, disability, and even mortality, imposing not only a heavy personal toll on patients but also a considerable economic burden on society.

Hip fractures in older adults are recognized worldwide as a significant public health issue, impacting quality of life and placing a substantial financial strain on both families and healthcare systems. While surgical fixation remains the standard approach for managing pertrochanteric femur fractures, treatment outcomes are influenced by factors such as fracture pattern, quality of reduction, implant stability, and underlying bone quality. [29]. The outcome in an adequately fixed fracture may be often compromised due to poor bone quality [29]. Recently, research has increasingly focused on enhancing overall bone architecture through pharmacological interventions, with teriparatide demonstrating encouraging results in both animal studies and clinical trials. [30-33)

Regarding the impact of teriparatide on osteoporotic hip fractures, existing literature presents mixed findings. A PubMed search identifies only a limited number of studies, most of which are retrospective in design and classify “elderly patients” as osteoporotic without applying definitive diagnostic criteria. Some reports suggest that teriparatide may promote faster fracture union. [34-36], while others didnt find improvement with Teriparatide therapy [37-39]. Han et al [40] analysis concluded that teriparatide can shorten the time required for fracture union in hip fractures. Teriparatide is a synthetic analog of parathyroid hormone (PTH), and its effects on bone depend on the dosage and pattern of exposure. Continuous exposure to PTH, such as in hyperparathyroidism, favors bone resorption over formation. In contrast, intermittent low-dose administration, as with daily teriparatide injections, stimulates bone formation to a greater extent than resorption. Although the precise molecular basis for the differing effects of PTH—catabolic with sustained exposure and anabolic with intermittent dosing—remains incompletely understood, several signaling pathways have been identified. The anabolic action of intermittently administered PTH is partly attributed to enhanced transcription of pro-osteoblastogenic growth factors such as insulin-like growth factor-1 (IGF-1) and fibroblast growth factor-2 (FGF-2). These factors promote osteoblast survival and proliferation, ultimately leading to the formation of new trabecular and cortical bone. This mechanism differs fundamentally from that of antiresorptive drugs, which act by suppressing osteoclast-driven bone resorption. Because bone resorption and formation are closely linked processes, this suppression also limits the generation of new bone.

.Group A started on INJ.TERIPARATIDE 20 mcg started from day5 and GroupB was started on vit D and calcium supplementation. There was significant improvement in fracture union time noted in the study group. Although

all the 30 patients achieved union by 24 weeks, and no union was seen at 6 weeks in both groups, the union rate was only 13.33% (two patients) in group A by 12 weeks, which was lower than that in the study group B, where the union rate was 56.25% (nine patients). This shows a statically significant improvement in fracture healing rates with teriparatide treatment (p=0.01) 0.01)A reduction in tip-apex distance indicated migration of helical blade plate progressively as the patient started to bear weight. The tip-apex distances of both groups were similar till 12 weeks of follow-up. But by 24 weeks, the tip-apex distance in group A was 22.57 ± 1.33, which was significantly much less than that in group B at 24.26±1.92 (p=0.031), suggesting earlier bony union and consolidation in the teriparatide group, which prevented blade migration, thus substantially reducing chance of screw cutout, hip pain, and implant failure (Table *2*). The change in the femoral neck shaft angle was recorded, and an increase in varus angulation was noted. The length of the femoral neck was also measured each time, and at 24 weeks significant shortening was observed in group A at 7.02±3.43 mm in comparison to 5.13±2.41mm in group B (p=0.02).

Radiological assessment done using the RUSH score revealed a score of 0 to start with as there was no evidence of union, and it was 30 in both groups by 24 weeks, suggesting complete radiological union in all patients both groups. No significant malunion, non-union, or any implant-related complication was seen in any patients at the end of 24 weeks.

Chesser et al [41] pilot study evaluated the use of teriparatide for six weeks in elderly patients with trochanteric fractures, aiming to determine the feasibility of conducting a large-scale randomized controlled trial. The authors noted several challenges that researchers might encounter when implementing a similar study design. Although detailed statistical analysis was not performed, all fractures in their cohort achieved union within 12 weeks post-surgery. In our prospective investigation focusing specifically on osteoporotic intertrochanteric femur fractures, teriparatide therapy was associated with an average reduction in time to union of approximately two weeks and an improvement in fracture healing rates at both 12 and 16 weeks.

The benefits of teriparatide extend beyond simply accelerating fracture healing. The newly formed bone exhibits increased density, greater osseous tissue volume, higher bone mineral content, and improved ultimate load to failure. The underlying pathophysiology appears to be multifactorial. Intermittent dosing has been shown to reduce both the number and volume of bone marrow adipocytes, suggesting a shift toward osteoblastogenesis and away from adipogenesis at the fracture site. Notably, osteoclast density remains unchanged, indicating that the drug promotes bone formation without enhancing bone resorption. [42].

Huang et al. observed that administering teriparatide in patients with osteoporotic pertrochanteric femur fractures was associated with improved functional outcomes at both three and six months of therapy. [35]. However, findings from Kim et al. have been inconsistent, with two separate studies yielding conflicting results regarding the efficacy of teriparatide therapy. [36,39], In their larger cohort study, they observed a marked improvement in Harris Hip Scores and a reduction in Visual Analogue Scale pain ratings as early as two months following the initiation of teriparatide therapy. [36]. In our cohort, no significant functional gains were observed at the three-month mark. By six months, however, the teriparatide group demonstrated markedly better performance. This finding aligns with earlier research indicating that teriparatide therapy can lead to significant improvements in bone mineral density at both the hip and spine when administered for 12 to 24 months. [45,46]. Sierra et al [47It was reported that a daily subcutaneous dose of 20 µg teriparatide increases lumbar spine BMD as early as six months, whereas a significant improvement at the hip typically appears only after about 12 months. Interestingly, in our study, the teriparatide group showed a marked increase in BMD at both the lumbar spine and the hip within just six months of treatment.

. We speculate that this early increase in hip BMD at six months may be related to altered bone mineral deposition patterns in osteoporotic patients with a contralateral hip fracture. This phenomenon could be explained by increased mechanical loading of the contralateral hip, or by systemic effects of the fracture healing process, which may stimulate bone formation at distant skeletal sites. Nevertheless, we acknowledge that our sample size is very small and studies with a bigger patient cohort might produce different results.

The success of treatment for osteoporotic intertrochanteric fractures largely depends on the implant's ability to maintain fracture stability until union occurs. However, poor bone quality frequently compromises outcomes, leading to complications such as varus collapse, screw migration, or excessive femoral neck shortening.. As opposed to Huang et al (20), In our study, no significant difference was observed between the groups in terms of medial migration of the blade or femoral neck shortening. Although varus collapse at six months was significantly greater in the non-Teriparatide group, the difference—approximately 1.5°—is unlikely to have meaningful clinical implications. A few other complications, such as bedsores and superficial wound infections, were more frequent in the Teriparatide group; however, given our limited sample size, definitive conclusions cannot be drawn. Further large-scale studies are warranted to explore these findings in greater depth.

Teriparatide therapy substantially increases the cost of treatment, an important factor to weigh against its benefits, particularly in developing countries. While an acceleration in recovery by approximately two weeks may not, on its own, justify its routine use in osteoporotic pertrochanteric fractures, the additional advantages—such as greater improvements in overall BMD and functional outcomes—may tip the balance in its favor.A significant

improvement in overall bone health [43] and reduction in the incidence of new and subsequent fragility fractures [44] reported in the literature further substantiate our claims.

Despite the projected advantages, several limitations of this study must be acknowledged. First, this was a preliminary investigation with a small sample size and short follow-up, limiting the ability to draw definitive conclusions regarding secondary outcomes. Second, the study was not blinded due to ethical considerations; although the outcome assessment criteria were objective, some degree of observer bias may have influenced data recording. Third, we did not compare Teriparatide therapy with bisphosphonates, which are more affordable alternatives for osteoporosis management. Finally, as radiological evaluations were performed at four-week intervals, the exact time to union could not be determined with precision.

RESULTS

Between October 2022 and October 2023, 30 patients with osteoporotic hip fractures underwent proximal femoral nailing. Of these, 15 received adjunctive teriparatide injections, while the remaining 15 were treated with calcium and vitamin D supplementation. The study cohort comprised 14 males and 16 females. The mean time from symptom onset to hospital admission was three days (range: 1–5 days). By the 24-week follow-up, all patients had achieved fracture union, and by 12 months, all demonstrated satisfactory Harris Hip Scores (HHS). Patients in the teriparatide group exhibited earlier bony union and consolidation, which minimized blade migration and significantly lowered the risk of screw cutout, hip pain, and implant failure.

Postoperative complications were minimal. One patient developed an aseptic superficial wound infection along the surgical suture line, which resolved with local wound care, antibiotics, and nutritional support. Three patients experienced grade 2 bedsores early during follow-up—one in the control group and two in the teriparatide group—which healed without complications. Additionally, one teriparatide-treated patient developed quadriceps wasting due to poor compliance with rehabilitation, which improved following regular counseling and prescribed exercises.

CONCLUSIONS

We conclude that teriparatide accelerates fracture healing and enhances bone mineral density in osteoporotic intertrochanteric hip fractures. While its use substantially increases treatment costs, the added benefits—including earlier fracture union, greater gains in bone density and mass, and improved functional outcomes—justify its use. Furthermore, its positive effects on overall bone health, beyond the fracture site, and its potential to lower the risk of new or subsequent fragility fractures support our recommendation for incorporating teriparatide into the management of osteoporotic intertrochanteric femur fractures.