



TERIPARATIDE FOR TREATMENT OF PATIENTS WITH BISPHOSPHONATE-ASSOCIATED ATYPICAL FRACTURE OF THE FEMUR

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Abstract

Introduction: Antiresorptive drugs such as bisphosphonates are widely used for the treatment of osteoporosis. Although effective for prevention of osteoporotic fractures, use of bisphosphonates is associated with rare but serious adverse events such as osteonecrosis of the jaw and atypical femur fractures (AFFs).

Methods: Patients who had been diagnosed with an atypical subtrochanteric and femoral fracture linked to the use of bisphosphonates were analysed. All underwent surgical intervention and teriparatide usage was suggested after surgery. Perioperative results, clinical And Radiographic Outcomes Were Considered Outcome Indicators.

Results: A total of 16 patients were included in the study. Depending on whether they had teriparatide medication or not they were divided into two groups. In the teriparatide treated group the mean time to bone union was 4.1 months and modified HHS at 6 months was 80.4

Conclusion: Post surgical management of AFF with teriparatide improves the fracture healing and improves the pain in patients with impaired bone turnover.

KEYWORDS: Teriparatide, Bisphosphonates, Fractures, Surgery

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1. INTRODUCTION

Bisphosphonates (BPs) are currently the most commonly used drugs for the treatment of osteoporosis. Their unique bone-seeking properties and subsequent uptake by osteoclasts result in sustained inhibition of bone resorption, even after cessation of treatment. They are the mainstay for the treatment of osteoporosis and have been shown to improve bone mineral density and reduce fractures.⁽¹⁾ Atypical femoral fractures are regarded as consequences of long-term bisphosphonate therapy with a low incidence. An AFF is a spontaneous or low-trauma, subtrochanteric or femur shaft fracture often complicated by delayed or nonunion (26%–39%) and bilateral occurrence. The age-adjusted incidence rate of AFF has been estimated to be 1.8 per 100 000 person-years in patients on bisphosphonate use under 2 years, increasing to 113 per 100 000 person-years with more than 8 years duration. Epidemiological data indicate that AFF account for less than 1% of all hip and femoral fractures.^(2,3)

The prolonged inhibition of bone remodelling brought on by the use of bisphosphonates may be linked to atypical fracture. Transverse to oblique fracture with thickening of the lateral cortex and spiking of the medial cortex are radiographic hallmarks of atypical fractures, which are typically located from the subtrochanteric region to the proximal femur. Also, osteoporotic individuals may experience delayed bone repair at the fracture site due to the lower bone turnover rate caused by bisphosphonate treatment. Anabolics may be used to reverse low bone turnover and encourage the production of new bone in an effort to address this problem. In patients with nonunion or delayed nonunion, teriparatide, a recombinant version of human parathyroid hormone, is thought to be an effective antiosteoporotic drug that promotes the production of new bone and

enhances bone healing. Although the precise mechanism has not been clarified, teriparatide treatment was reported to revive bone remodelling following the use of bisphosphonates and may be useful in encouraging bone repair.^(4,5,6,7)

A major concern about the atypical femoral fracture (AFF) has been determining the most appropriate medical management after the fracture has been surgically evaluated and/or repaired. The preferred treatment for atypical femoral fractures (AFFs) is intramedullary nails. According to certain research, the surgical outcomes of AFF are worse than those of normal femoral fractures.

The risk of reoperation was four times higher in patients with AFF due to periimplant instability⁽⁸⁾. The advantages of teriparatide for patients with atypical fractures have been covered in numerous case reports and series investigations. To further elucidate this matter, more information on the course of treatment for atypical fractures is critically required. Our study's objective is to determine the surgical outcome of atypical subtrochanteric and femoral fractures associated with the use of bisphosphonates in patients receiving teriparatide medication or not.

2. METHODOLOGY:

Patients who had been diagnosed with an atypical subtrochanteric and femoral fracture linked to the use of bisphosphonates were analysed. Patient's clinical symptoms, medication history, radiographic features, surgical techniques, therapeutic results, and followup findings were maintained. The study included 16 female patients who had experienced minor injuries and reported thigh pain. The characteristics of an atypical fracture, such as a transverse or short oblique fracture without bone comminution, were consistent with radiographic findings. After an atypical fracture was identified in each of these individuals, bisphosphonate

treatment was stopped, but calcium infusion still continued. All patients had surgery, which involved internal fixation using an intramedullary device. Following surgery, teriparatide at a once-daily 20 mcg dose was suggested for osteoporosis maintenance and improved bone repair.

Radiographic Outcome:

The radiological evaluation was based on follow-up radiographs taken immediately after surgery as well as at 1, 2, 3, 6, and 9 months and 1 year afterwards. The United States Food and Drug Administration (US FDA) defines nonunion as a fractured bone that has not fully healed within nine months of the injury and that has not progressed in healing on serial radiographs for three months in a row. The absence of bone union evidence at postoperative six

months was used to characterise delayed union.

Functional Outcomes:

Independent reviewers conducted retrospective functional evaluations over the phone using the modified Harris Hip Score (HHS) at 3, 6, and 1 year after surgery.

Data Analysis:

Data was analysed using SPSS 23.0 version. The Mann-Whitney U test and Fisher's exact test were used in the statistical analysis. Level of significance was set at $p < 0.05$.

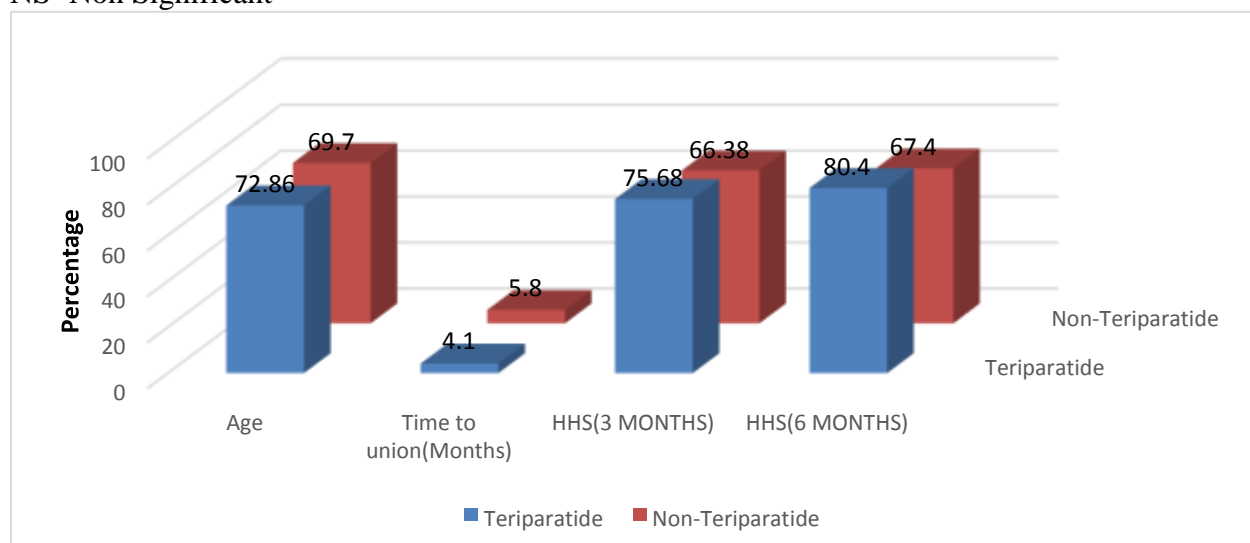
Results:

A total of 16 patients were recruited for the study. Every patient had an exposure to bisphosphonates – alendronate, for at least a couple of years.

TABLE: THE RESULTS OF OUR STUDY HAVE BEEN DESCRIBED BELOW

	Teriparatide	Non-Teriparatide	p-value
Age	72.86	69.74	0.724(NS)
Time to union(Months)	4.1	5.8	0.082(NS)
Union at 6months	6	5	0.824
Implant Failure	0	1	1
Modified HHS at 3 months	75.68	66.38	0.312
Modified HHS at 6 months	80.4	67.4	0.01*

NS=Non Significant



3. DISCUSSION:

In the present study all the AFF were treated by internal fixation using intramedullary nail. Patients were divided randomly into those receiving teriparatide and those without receiving teriparatide. Following surgery, teriparatide (20mcg) once daily was administered to the teriparatide treated group. In comparison to the non teriparatide treated group, the teriparatide treated group displayed superior outcomes with a higher modified HHS at 6 months following surgery. All of the patients in the study were female and they had been on alendronate for a mean of 2.9 years. In our study, Teriparatide treatment allowed the majority of patients to achieve bone union within 6 months with a mean of 4.1 months. The mean HHS at 6 months post surgery was 80.4 in the teriparatide treatment group while it was 67.4 in the non teriparatide treated group.

Teriparatide medication increases the bone healing and union for individuals with AFF despite the fact there was no significant difference in the p-values between the two groups. Although the use of bisphosphonates has raised concerns about atypical fractures, osteoporosis related problems can still result in morbidity and mortality.

Our study has several advantages. The radiologists who scored the primary outcome of bone healing were blinded to the allocation. All the patients were followed up and analysed. It is a prospective study with a long follow up.

Despite the various advantages, the study also had limitations. The sample size was small and the study included only female patients. Female patients may acquire bisphosphonates several years sooner than male patients due to the developmental course of their usage and their use as a treatment for postmenopausal osteoporosis, which will result in a longer exposure among female patients. This could explain why male patients rarely

experience unusual femur fractures. Therefore, further research, involving more number of patients are recommended.

4. CONCLUSION:

Although there is no evidence based indication for teriparatide to enhance healing of AFF but faster healing with teriparatide for surgically managed AFFs is seen in the limited data available. Patients treated with teriparatide may benefit from pain relief, hip function rehabilitation and fracture repair. The treatment is safe and well tolerated among the patients. However, due to the low incidence of such AFFs the results should be interpreted with caution.

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