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Surgical outcome assessment in femoral fracture patients with or without teriparatide treatment

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Abstract:

Introduction: Femoral fracture and atypical subtrochanteric fracture are thought to be uncommon side effects of long-term bisphosphonate treatment. Delay in bone healing may be caused by a decreased rate of bone turnover. Limited research has shown that teriparatide therapy may counteract the effects of bisphosphonates and promote bone repair.

Methods: A retrospective assessment of individuals with atypical subtrochanteric and femoral fractures associated with the use of bisphosphonates were examined. There were 18 female patients signed up. The characteristics of an unusual fracture were congruent with the radiographic findings. All underwent surgical intervention, and teriparatide usage was suggested after surgery. Perioperative results, clinical, and radiographic outcomes were all considered outcome indicators.

Results: Of the 18 female patients that were enrolled, 13 had proximal femoral fractures, 18 subtrochanteric fractures, and 6 had bilateral fractures. The majority of fractures had prodromal thigh discomfort. Without any major difficulties, an intramedullary fixation method was used to treat all patients. Depending on whether they had teriparatide medication or not, the patients were split into two groups. In the teriparatide-treated group, the mean time to bone union was 4.5 months, compared to 6.3 months in the control group (p=0.084). At six months following surgery, the modified Harris Hip Score and Numerical Rating Scale mean

values were considerably higher in the teriparatide-treated group. Eight patients could still walk after a year of monitoring, just as they could before the unusual fracture.

Conclusions: Teriparatide medication in individuals with atypical fractures may aid in hip function restoration, fracture healing, and pain alleviation in this patient population with impaired bone turnover.

Keywords:, Bisphosphonates, femur fractures , Osteoporosis, subtrachanteric, Teriparatide

Introduction:

Atypical femoral fractureand subtrochanteric fracture are regarded as consequences from long-term bisphosphonate therapy with a low incidence. A prodrome of thigh discomfort, little trauma or perhaps no trauma, and specific radiological characteristics are among the clinical symptoms and indicators (1,2).

The prolonged inhibition of bone remodelling brought on by the use of bisphosphonates may be linked to atypical fracture (3). 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 (4). Additionally, osteoporotic individuals may experience delayed bone repair at the fracture site due to the lower bone turnover rate caused by bisphosphonate treatment (5). 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 anti-osteoporotic drug that promotes the production of new bone and enhances bone healing (6). 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(7).

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 (8). According to Bogdan et al.(9), patients with entire AFF had surgical treatment at a slower rate of healing compared to those with normal femoral fractures and had a greater rate of non-union, with 13% requiring revision surgery on average 11 months later. The risk of reoperation was four times higher in patients with AFF due to peri-implant instability. 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.

Methodology:

Patients who had been diagnosed with an atypical subtrochanteric and femoral fracture linked to the use of bisphosphonates were retrospectively analysed. Patient's clinical symptoms, medication history, radiographic features, surgical techniques, therapeutic results, and follow-up findings were maintained. The study included 18 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.

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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 g dose was suggested for osteoporosis maintenance and improved bone repair.

Outcome measures

Perioperative assessment

Clinical assessment was done based on the incidence of perioperative complications and their causes, such as wound problems, anesthesia-related morbidity, or even mortality.

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. Two independent observers evaluated fracture union, delayed union, and implant material failure using radiographic images from both lateral and anteroposterior perspectives. 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 (10). 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, as well as the Numerical Rating Scale (NRS) pain score at the postoperative follow-up and at 3, 6, and 9 months after surgery. The patients were divided into one of four groups depending on their level of walking ability at the 1-year postoperative follow-up: walking without assistance, walking with a cane, walking with a walker, and not walking. With a maximum score of 100 points, the modified HHS is a functional evaluation scale for the hip that assesses pain, mobility, daily activities, and range of motion (11). For the purpose of evaluating pain, the NRS pain score, which ranges from 0 to 10, was utilised. The scale reflects the patients' subjectively perceived pain ratings, which range from 0 (no pain) to 10 (the greatest conceivable agony).

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 18 patients, with 24 fractures were recruited for the study. Every patient had an exposure to bisphosphonates – alendronate, for at least a couple of years. The clinical variables of the study population is summarized in Table 1.

The mean of the modified HHS, which measures functional outcome, was 78.79 in the teriparatide-treated group at postoperative six months and 69.25 in the non-teriparatide-treated group, showing a significant difference($p=0.011$) The NRS at 6 months after surgery indicated a mean of 2.74 in the group treated with teriparatide and 3.99 in the group not treated with teriparatide, which was a significant difference (p value = 0.035). Eight patients had the same walking capacity as before to the atypical fracture, according to an assessment of walking ability at the 1-year postoperative follow-up (Table 2).

Table 1: Clinical characteristics of the two groups

	All	Teriparatide	Non-teriparatide	P value
Atypical fracture	24	12	12	
Age	72.15	71.56	68.25	0.872 (NS)
Proximal femur	8	4	4	1 (NS)
Subtrochanteric fracture	12	6	6	1 (NS)
Time to union	5.2	4.5	6.3	0.084 (NS)
Union at 6 months	11	7	5	0.712
Implant failure	2	0	2	1

*=Significant; NS=Not significant

Table 2: Functional outcomes between groups

Modified Harris Hip Score (HHS)	All	Teriparatide	Non-teriparatide	P value
Post operative 3 months	68.25	73.10	64.16	0.213 (NS)
Post operative 6 months	75.32	78.79	69.25	0.011*
Post operative 1 year	83.64	86.38	79.11	0.257(NS)
Numerical Rating scale				
Post operative	7.67	7.37	7.7	0.385 (NS)
Post operative 3 months	4.02	3.97	4.46	0.586 (NS)
Post operative 6 months	3.64	2.74	3.99	0.035*
Post operative 9 months	2.01	1.53	2.6	0.252(NS)
Post operative 1 year	1.24	1	1.52	0.736
Recovery to pre-OP walking ability	8	6	2	0.326(NS)

*=Significant; NS=Not significant

Discussion:

In the present study, internal fixation with intramedullary osteosynthesis was used to treat 18 female patients with 24 fractures. In comparison to the non-teriparatide-treated group, the

teriparatide-treated group displayed superior outcomes with a considerably higher modified HHS and lower NRS at 6 months following surgery. Teriparatide's positive effects on bone remodelling caused by chronic bisphosphonate treatment may explain why it is beneficial to use it.It is thought that atypical subtrochanteric and femoral fractures caused by long-term bisphosphonate therapy for osteoporosis are stress fractures brought on by low or no trauma. The average time a patient had bisphosphonate medication was often greater than 4 years (12,13). All of the patients in this study were female, and they had been on alendronate for a mean of 3.04 years (ranging from 2.1 to 5.8 years). Although some investigations have suggested a potential mechanism, the precise aetiology of an atypical fracture has not been conclusively established (14). We can infer from the available data that decreased bone remodelling may also have an adverse influence on crack removal, which may result in a high risk of delayed union or even nonunion. In our study, teriparatide treatment allowed the majority of patients to achieve bone union within 6 months, with a mean of 4.5 months. Teriparatide medication may enhance bone healing and union for individuals with atypical fractures, despite the fact that there was no significant difference in the p values between the 2 groups. Even if the use of bisphosphonates has raised concerns about atypical fractures, osteoporosis-related problems including hip fractures can still result in morbidity and mortality. The usage of bisphosphonates has been shown to reduce the likelihood of hip fracture by 30%. (15,16) In a review of data from the US FDA Adverse Event Reporting System (FAERS) (from 1996 to 2011), Edward etal.(17) reported the incidence of bisphosphonate-associated non-healing femoral fractures and came to the conclusion that the benefits of bisphosphonate use outweigh the risk of atypical femoral fractures by a factor of a hundred.

Certain limitations of the study further need mention. Any comparison between the two treatment groups could be weaker as a result of the small sample size and retrospective study methodology. Additionally, all patients received the teriparatide therapy recommendation; nonetheless, the final decision was with the patient and family, which raised the possibility of bias. Another limitation is that only females are included. 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 arerecommended.

Conclusion:

Patients with atypical fractures who are treated with teriparatide may benefit from pain alleviation, hip function rehabilitation, and fracture repair. Although the data were not statistically significant, using teriparatide may also enhance the bone union rate.

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