International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 02 Issue 04 April 2017, ISSN: 2455-8737, Imp. Factor - 4.102
Available online at - www.ijirms.in

Open Access Journal | Research Article | DOI: 10.23958/ijirms/vol02-i04/11

Atypical Femur Fracture: Correlation between Bisphosphonates Users and Nonusers

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Abstract

Medications to treat and prevent osteoporosis, such as bisphosphonates, are now being increasingly used. This drug can prevent common osteoporotic fractures in patients with osteoporosis, particularly in the hip and vertebrae. But recently it has been found that bisphosphonate-related suppression of bone remodeling may adversely influence bone strength. The pathogenicity of atypical femoral fractures is due to the accumulation of microdamage which leads to homogeneity in bone tissue and there is low homogenecity due to use of bisphosphonates and subsequently leads to lower bone quality. However, the association between long-term use of bisphosphonates and atypical femoral fractures is still doughtful and lots of studies have showed variability in relative risk factors. Stress fractures which have been well recognized to be caused by bowing deformity may also be classified as atypical femoral fractures. Therefore this study was done to investigate and to compare clinical characteristics and surgical outcome of atypical femoral fractures associated with patients on bisphosphonates and those of fractures not associated with bisphosphonates use. ***Material and Methods*:** A total of 46 patients who had been operatively treated for a complete atypical femoral fracture were identified. Patient information, including clinical manifestations, medication history, radiographic characteristics, operative methods, treatment outcome and follow-up results were recorded. Bisphosphonates use was stopped after atypical fracture was diagnosed, but calcium supply was continued. Perioperative clinical assessment was performed. Radiological assessment was done by taking radiographs postoperatively at 1, 2, 3, 6, 9 month and 1 year post operation. ***Results*:** A total of 46 patients with atypical femoral fracture were enrolled in the study. of which 41 patients were having history of bisphosphonate use while 5 were not using the drug. Average Duration of Bisphosphonate use (in years) was 3.85.Time to union in patients on bisphosphonates was 5.23 months while 24(52.17%) achieved union at six months. In one patient implant failure was found. Neither in patients who were nor taking bihosphonate drugs. Out of 41 biphosphonate group patients 24(52.1%) achieved complete bony union within 6 months, while in non bisphosphonate user complete union in six months was 4 (80%). ***Conclusion***: In conclusion of 46 patients 24(52.17%) patients on biphosphonats showed bony union and 4 (80%) showed bony union within 6 months after the index surgery. There was no difference in bony union rate between the biphosphonate group and the non-biphosphonate group.

Introduction

Osteoporosis is associated with significant morbidity and mortality.[1] Medications to treat and prevent osteoporosis, such as bisphosphonates, are now being increasingly used. This drug can prevent common osteoporotic fractures in patients with osteoporosis, particularly in the hip and vertebrae.[2] Bisphosphonates are anti-resorptive agents approved by the FDA, and they increase bone mineral density and prevent osteoporotic-related fracture.[3] But recently it has been found that bisphosphonate-related suppression of bone remodeling may adversely influence bone strength.[4] It has been reported that long-term BP use may affect the incidence of atypical femoral fractures.[5] A typical femoral fracture is defined as caused by a high-energy trauma, such as a road traffic accident, that is frequently accompanied by a third fragment and shape of comminuted fracture. However, atypical femoral fractures are defined as atraumatic or low-trauma fractures located in the subtrochanteric region or femoral shaft.[4] The pathogenicity of atypical femoral fractures is due to the accumulation of micro damage which leads to homogeneity in bone tissue and there is low homogeneity due to use of bisphosphonates and subsequently leads to lower bone quality.[6] Long-term use of bisphosphonates causes premature aging of bone, making them more brittle and less likely to impede crack tip progression.[7] However, the association between long-term use of bisphosphonates and atypical femoral fractures is still doughtful and lots of studies have showed variability in relative risk factors.[8,9] The American Society for Bone and Mineral Research Task Force in 2013 revised the case definition of atypical femoral fractures in which they deleted the clause associated with the use of pharmaceutical agents such as BPs, glucocorticoids, and proton pump inhibitors and under this definition, stress fractures which have been well recognized to be caused by bowing deformity may also be classified as atypical femoral fractures.[4,10] Delayed or failed fracture

healing is a major concern after fracture stabilization in patients taking bisphosphonates. However very less data is available for atypical femoral fracture occurring without use of bisphosphonates. Therefore this study was done to investigate and to compare clinical characteristics and surgical outcome of atypical femoral fractures associated with patients on bisphosphonates and those of fractures not associated with bisphosphonates use.

Material and Methods

This study was conducted in The Dept. of Orthopaedics at Meenakshi Medical College Hospital and Research Institute Enathur Kanchipuram. A total of 46 patients who had been operatively treated for a complete atypical femoral fracture were identified. Atypical femoral fractures were defined by characteristic radiographic findings according to the criteria of the 2013 American Society for Bone and Mineral Research Task Force.[4] All fractures were occurred with a history of minimal or no trauma. Minimal trauma was defined as a slip or fall from a standing height or less.

This project was approved by the Research Ethics Board of the institute. Informed consent was taken from all the cases involved in the study.

Patient information, including clinical manifestations, medication history, radiographic characteristics, operative methods, treatment outcome and follow-up results were recorded. Bisphosphonates use was stopped after atypical fracture was diagnosed, but calcium supply was continued. Surgical intervention was performed for all patients via internal fixation.

Perioperative clinical assessment was performed based on occurrences of perioperative complications and their causes which includes wound problems, anesthesia-related morbidity and mortality.

Radiological assessment was done by taking radiographs postoperatively at 1, 2, 3, 6, 9 month and 1 year post operation. Delayed union, non union, implant material failure, fracture union was analysed using radiographic images. Non union was defined as a fractured bone that has not completely healed within 9 months post fracture. Delayed union was defined as the lack of bone union evidence at postoperative 6 months. Pain score at the postoperative follow-up and at 2, 3, 6, and 9 months, and 1 year post-operation was done. Walking ability was assessed.

Data Analysis

Data were expressed as mean ±SD. Mean values were assessed for significance by unpaired student –t test. A statistical analysis was performed using the Stastical Package for the Social Science program (SPSS, 21.0). Frequencies and percentages were used for the categorical measures. Probability values $p < 0.05$ was considered statistically significant.

Results and Observation

A total of 46 patients with atypical femoral fracture were enrolled in the study of which 41 patients were having history of bisphosphonate use while 5 were not using the drug. Average Duration of Bisphosphonate use (in years) was 3.85. Proximal femur fracture was seen in 15 patients and subtrochantaric fracture was seen in 26 patients who were taking biphosphonates. Time to union in patients on bisphosphonates was 5.23 months while 24(52.17%) achieved union at six months. In one patient implant failure was found. In patients neither who were nor was taking bihosphonate drugs. Mean age 69.13. There were 2 males and 3 females. Proximal femur fracture and Subtrochanteric fracture was seen in 1 and 4 cases respectively.

Table 1: Demographic and clinical characteristics of the 2 patient groups

	Biphosphonates users	Without biphosphonates
Atypical fracture	41	5
Age (yr)	68.14	69.13
Male	19 (46.34%)	2 (40%)
Female	22(53.65%)	3(60%)
Duration of Bisphosphonate use (yr)	3.85	0
Proximal femur fracture	15	1
Subtrochanteric fracture	26	4
Time to union (month)	5.23	4.16
Union at 6 months (%)	24(52.17%)	4 (80%)
Implant failure	1	0

Out of 41 biphosphonate group patients 24(52.1%) achieved complete bony union within 6 months, while in non bisphosphonate user complete union in six months was 4 (80%).

Table 2: Characteristics of fracture

Injury mechanism	Biphosphonate group n=41	Non-Biphosphonate group n=5
Fall-down	18 (43.90%)	4 (80.0%)
Slip-down	21 (51.21%)	1 (20.0%)
No trauma	2 (4.88%)	0 (0%)

Of the total 41 patients from bisphosphonate group 18 (43.90%) fractures were due to fall down, 21 (51.21%) due to slip down and 2 (4.88%) were not having any trauma. In non-bisphosphonate group 4 (80%) fractures were due to fall down and 1 (20%) was due to slip down. Out of 4 of the non-BP group, 1 had refracture and underwent revision surgery.

Discussion

Prolonged use of bisphosphonate for osteoporosis is considered to be a stress fracture after minor or even no trauma and atypical sub trochanteric and femoral fracture are the most atypical femoral fracture. Mean duration of bisphosphonate use was considered usually more than 4 years. But different studies have shown different values.[11,12] In our study duration of Bisphosphonate use was 3.85 years. According to American Society for Bone and Mineral Research 2013, stress fractures, occurring without a history of consuming biphosphonates drugs may also be classified as atypical femoral fractures. In our study of 46 patients with atypical femur fracture 41 patients with a history of consuming biphosphonates drugs for at least 3 years and 4 patients without a history of biphosphonates medication are recruited. Thus the rate of atypical femur fracture in patients without a history of biphosphonates medication was 10.86% in our study. It was in accordance with the study by Tan et al. who reported the rate of atypical femoral fractures without biphosphonates use was 8% in their study of 50 patients.[13]

The exact pathogenesis of atypical fracture has not been well understood. Some proposed that the effect of decreased bone remodeling may also lead to reduced crack removal.[9,14] which may result in a delayed union rate or non union of the bones.[15] In our study time to union at 6 months was 24(52.17%) foe bisphosphonates users while for non bisphosphonates group it was 4 (80%). In a study by Huang et al.[16] he found after 1 month pain and tenderness improved, after 9 months symptoms disappeared and after 15 months, fracture line completely healed in a study on female who was using bisphosphonates for atleast 3 years. Ekström et al reported that half of their patients with subtrochanteric fracture could not recover to their pre-fracture level of activities and they had a high mortality rate, up to 25%, at the 2-year follow-up.[17] In a study by Yeh W-L et al.[18] 10 atypical fractures (62.5%) presented good bone union within 6 months, 5 fractures (31.25%) were recognized as delayed union, and 1 patient had non union with implant failure. An earlier study by Egol KA et al.[19] evaluated 41 atypical, low-energy femoral fractures associated with more than 5 years of bisphosphonate use, reported that 98% (40/41) showed radiographic union at a mean of 8.3 months.

Asians have differences in femur anatomy with higher rates of bowing, compared to western populations.[20] In some studies it has been suggested that due to anteriorly and laterally bent shape of the femur stress concentration on the diaphysis may be an important causative factor of the atypical fracture.[10,12]

The association between atypical femoral fractures and biphosphonate drug use is still controversial. Biphosphonate drugs seem to increase risk of atypical fractures, and greater risk is related to longer duration of management and risk is declined after stopping biphosphonate medication.[21] Also atypical fractures have also seen in patients who have never been exposed to bisphosphonate.[9] Donnelly et al.[22] observed that while biphosphonate treatment may be an important risk factor for atypical fractures but it cannot be the sole risk factors.

Our study has some limitations because there were a limited number of patients and large number of patients cannot be included in the study because of relatively rare injury type also we could not investigated the functional outcome

Conclusion

In conclusion of 46 patients 24(52.17%) patients on biphosphonats showed bony union and 4 (80%) showed bony union within 6 months after the index surgery. There was no difference in bony union rate between the biphosphonate group and the non-biphosphonate group. Implant failure was observed in one fracture using biphosphonates.

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