

Original Article

Prevention of subsequent hip fractures among geriatric population with use of bisphosphonates.

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Abstract

Background: In the geriatric population, osteoporotic or fragility hip fractures hold a significant health burden and are scrupulously linked with a greater possibility of morbidity and mortality among this population group, even though there is an increased incidence of subsequent hip fractures. Bisphosphonates are extensively used in treating and preventing fragility hip fractures as prophylactically.

Methodology: From March 2014 to February 2020, a total of 2430 patients were enrolled with their first hip fracture. After determining the second hip fracture, a comparison between non-compliant and compliant bisphosphonate users (Ibandronic Acid) was conducted. Medication Possession Ratio of more than 80% post first hip fracture treatment was defined as bisphosphonates compliant user.

Results: Among 2430 patients, 65.2 years was the mean age at the first hip fracture (ranging from 51 to 91 years). A total of 146 (6.0%) patients suffered from second hip fractures at a mean duration of 29.45 months post first hip fracture. 2nd hip fracture was observed in only 3.5% (30/860) of compliant bisphosphonate users compared to non-compliant users with 7.4% (116/1570).

Conclusion: Among the geriatric population, the use of bisphosphonate (Ibandronic Acid) has a significant impact on preventing subsequent hip fractures. Hence this emphasizes the need to use bisphosphonates in clinical practice to help to minimize the burden of hip fractures.

Keywords

Bisphosphonate, Compliance, Osteoporosis, Second Hip fracture, Fragility Hip Fracture.



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Introduction

Fragility hip fractures have become a universal health problem in the ortho-geriatric population¹. Usually, it has a poor impact on patients because it may interfere with the quality of life, like diminished activity level, increased risk of second hip fracture, and adversely affect the increased risk of mortality among this group of population^{2,3}. Among our Pakistani geriatric population, 12.9% of women suffer from osteoporosis, and the proportion of patients with osteoporosis has increased with time. This could invariably result in a poor quality of life among this group of people⁴.

An osteoporotic patient requires comprehensive care, interventions requiring multidisciplinary actions, and a rigorous rehabilitation outline with exercises oriented towards specific areas of intervention. A different group of bisphosphonates is now frequently used to treat osteoporosis universally to prevent fragility fractures. Orthopedic surgeons and primary care physicians encourage using bisphosphonate because it prevents osteoporotic fractures^{5,6}.

The overall incidence of getting a second hip fracture is lower than that of suffering from the first hip fracture. One year mortality rate after 1st hip fracture is 15.9%, whereas five years mortality rate is 45.4%. On the other hand, the one-year mortality rate after a second hip fracture is 24.1%, whereas that of five-year mortality is 66.5%^{7,8}. There is a lack of published data for recurrent hip fractures worldwide, fewer still in the Asian population and nothing of significance in the Pakistani population. Subsequent hip fractures among the geriatric population are reported variably from 2-10%, but its incidence reported in the Asian population is about 8.6% after 1st hip fracture^{3,7,9,10}.

Many guidelines like American Association for Health and Clinical Excellence recommend using Bisphosphonates to prevent subsequent hip fractures after initial hip fracture^{8,11}. Furthermore, some studies have been published which support the use of Bisphosphonates among the geriatric population to prevent subsequent fragility hip

fractures, and its use has been increasing exponentially in Asia^{5,12,13}.

Keeping in mind the dearth of local literature on recurrent hip fractures, the objective of our research was to rectify the incidence of subsequent hip fractures among a geriatric group of the population and its correlation with whether it is consistent bisphosphonate consumption reduces the chances of second hip fracture.

Methodology

Prospective data of 2880 hip surgeries, including neck of femur and/or intertrochanteric fractures, were collected from March 2014 to February 2020 in individuals over 50 years of age who were admitted to the Orthopedics Department of Liaquat National Hospital and Medical College, Karachi, Pakistan. Ethical approval was obtained from the departmental ethics committee and written informed consent was obtained from each patient.

The Inclusion criteria of our study were patients 50 or more than 50 years of age, who had a hip fracture from low energy trauma, and who were fixed surgically for the first time and were monitored for a minimum of 3 years in outpatient follow-up. A hip fracture from low energy trauma is defined as occurring due to a trauma force equal to or less than a fall at standing height.

42 patients who had pathological fractures and 76 patients with prior hip fixation surgery for hip fractures were excluded from the study. A total of 332 patients were lost to follow-up. Thus, 2430 patients met the inclusion criteria and were followed for at least 3 years postoperatively, with a mean follow-up of 38-46 months (ranging from 1 to 48 months).

Medication possession ratio (M.P.R.) was used to evaluate compliance of bisphosphonates (Ibandronic Acid), measured in 3 years of treatment post first hip fracture^{14,15}. By definition, M.P.R. is the total number of days of bisphosphonate supply divided by the total number of days of follow-up (which is 1095 days in this study). An M.P.R. of more

than 80% for a year after a hip fracture was the criterion used to identify the patients who were compliant bisphosphonate users. While if any patient had a subsequent hip fracture after 6 months of 1st hip fracture, they were considered non-compliant bisphosphonate users.

The enrolled patients underwent surgical intervention with sliding hip screws, cannulated hip screws or proximal femur nails for internal fixation, and hip arthroplasty consisting of total hip arthroplasty or bipolar hemiarthroplasty. Postsurgical mobilization consists of wheelchair mobilization or highly secured weight bearing is achievable with the help of wheelchairs, crutches, walking aids, or walkers.

Following discharge from the hospital, patients were kept on routine follow-ups in clinics at 2, 6 weeks, 3 months, 6 months, and at 1 year, with 6 months intervals till 3 years. Similarly, the frequencies of second hip fractures were compared in both groups, including the type of surgery, BMI, Gender, age, ambulatory status prior to surgery, and Anesthesia risk stratification by the Anesthesia Society of America (A.S.A.) scoring system. Bone mineral density scans of total hip and bisphosphonate therapy (Ibandronic Acid) were recorded to find the link between these parameters and the risk of a second hip fracture. Ibandronic acid (3mg/3ml with 3 months interval for 3 years.) as bisphosphonates quarterly was used in the study with intravenous infusion of injection All the patients were explained in detail the use of Ibandronic acid with its benefits and side effects.

The patient's comorbidities were recorded as follows: congestive heart failure, diabetes mellitus, hypertension, liver dysfunction, respiratory dysfunctions, and myocardial disease, angina, and neurological status, and kidney dysfunction, gastrointestinal or psychiatric issues. These comorbidities were stratified using the Modified Charlson Comorbidity index to determine overall

health status. Scoring was done as follows: 3 points for chronic liver failure, 2 points for cerebrovascular accidents or neoplasms, 1 for congestive heart failure, pulmonary disease, myocardial infarction, dementia, deep venous thrombosis, arthritis, ulcers, diabetes mellitus, and peripheral arterial disease. Scoring varied from 0-15, with higher scores indicating poor health status.

Statistical analyses determined compliance with bisphosphonate usage to reduce the second hip fracture. Two groups were made: second hip fracture and non-fracture groups, of which univariate analysis was performed to determine the confounding factor. A Chi-square test was applied to determine the statistical differences in categorical parameters between the two groups. Student t-test was applied for continuous variables with a p-value ≤ 0.05 ; binary logistical regression was used to determine the decrease in the incidence of subsequent hip fractures among the compliant user of bisphosphonate. SPSS version 21.0 was used for analysis.

Results

Among 2430 patients, the mean age at the first hip fracture was 65.2 years (ranging from 51 to 91 years). Patients who suffered from 2nd hip fractures were 146 (6.0%) at a mean duration of 29.45 months, ranging from 1 to 48 months after 1st hip fracture. No significant side effects were observed in any patient with Bisphosphonate (Ibnadronic Acid) in our study.

Out of 860 compliant users, there were 242 males and 618 females, and the average age at first hip fracture was 65.98 years, and the average BMI was 27.7 kg /m². The non-users group consisted of 1570, of which 420 were males and 1150 were females, and the mean age at first hip fracture was 64.9 years, and the mean BMI was 29.2 kg / m² (Table 1).

Table 1: Features of Compliant User and Non-Compliant User.

Variables	Compliant User (n=860)	Non-Compliant User (n=1570)	Total (n=2430)	P-value
Age (years)	65.98±9.8	64.91±9.7	65.29±9.77	0.406
BMI (kg/m²)	27.7±5.4	29.2±5.6	28.71±5.59	0.312
Gender	Male	420	662	0.603
	Female	618	1768	
Type of Fracture	Femoral Neck Fracture	296	806	0.493
	Intertrochanteric fracture	564	1624	
Type of Surgery	Internal Fixation	614	1756	0.617
	Hemi/Total Arthroplasty	246	674	
2nd Hip Fracture	Yes	30	146	0.006*
	No	830	2284	

*p<0.05 is considered significant.

Incidence of 2nd hip fracture was observed in only 3.5% (30/860) of the compliant user of bisphosphonate compared to the non-compliant user with 7.5% (116/1570). Cumulative frequency for subsequent hip fractures was recognized as 1.1% (26/2430) in 1st year, 1.4% (34/2430) in 2nd year, 1.6% (38/2430) in 3rd year, and 2.0% (28/2430) at 4th years.

In the compliant group, 3.5% (30/860) of subsequent hip fractures were observed, while the non-compliant group had an incidence of 7.4% (116/1570) with a p-value of 0.006. Using Chi-square test, hematological disease (p=0.039), renal disease (p=0.003) and compliant user of bisphosphonates (p=0.006) resulted in a p-value ≤ 0.05 (Table 2).

Table 2: Univariate Comparison among Second Hip Fractures and No Subsequent Fracture Group.

Variables	No Subsequent Hip Fracture (n=2284)	Second Hip Fracture (n=146)	P-value
Age (Years)	65.23±9.78	66.21±9.58	0.406
Gender	Male	42	0.763
	Female	1664	
BMI (kg/m²)	28.75±5.60	28.07±5.42	0.312
Fracture Type	The neck Femur Fracture	46	0.756
	Intertrochanteric fracture	1524	
Surgery Type	Internal Fixation	112	0.381
	Hemi/Total Arthroplasty	640	
Charlson's Comorbidity Index	1.55±1.07	1.61±1.38	0.723
BMD	-3.2 ± 0.71	-3.6 ± 0.69	0.000*
Bisphosphonate (Ibandronic Acid)	User	30	0.006*
	Non-User	116	

Co-morbid conditions	Hypertension	1272	82	0.937
	CCF/IHD	40	04	0.385
	Cerebrovascular Disease	142	12	0.457
	Diabetes Mellitus	1114	56	0.084
	Chronic Pulmonary Disease	178	12	0.895
	Liver Disease	86	12	0.068
	Hematological diseases	20	06	0.039*
	Malignancy	74	08	0.304
	Renal Disease	126	22	0.003*
	Gastrointestinal Disease	38	02	1.000
	Psychiatric Disease	122	04	1.000

Using multivariate analysis, independent variables such as gender, B.M.I., age, kidney diseases, M.P.R., and hematologic disorders were tested for cofounders. Kidney dysfunction Odd ratio was 3.039; 95% confidence intervals (1.525-6.057) and hematologic disorders (OR, 4.851; 95% CI, (1.306-18.027) were closely linked with second hip fracture (Table 3). Therefore, compliant consumption of bisphosphonates decreased the incidence of future hip fracture (OR, 2.207; 95% CI, 1.235-3.944) (Table 3 and Figure 1).

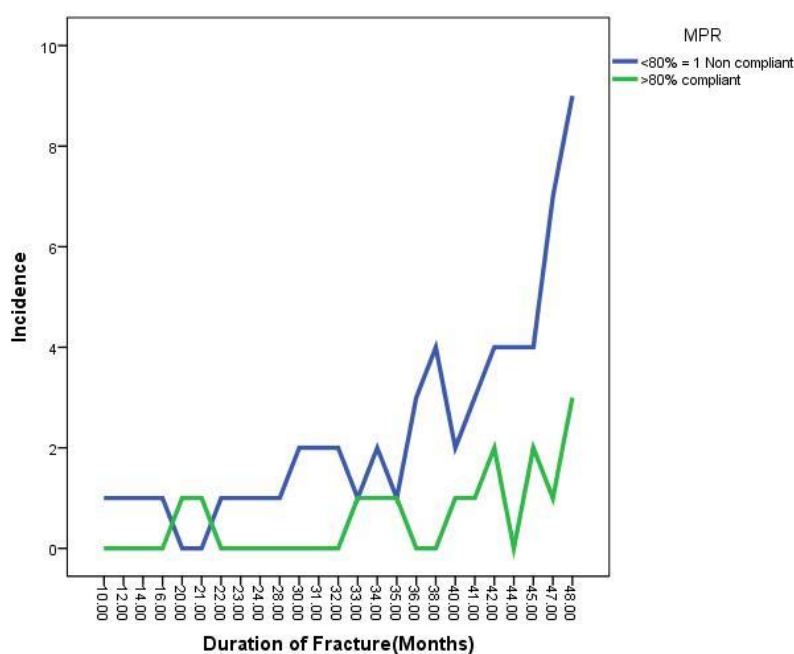


Figure 1: Binary Logistic Survival curve per medication possession ratio (M.P.R.).

Table 3: Logistic Regression Analysis for second hip fracture.

Variables		Adjusted OR (95% CI)	p-value
M.P.R.	Compliant User	1	0.008
	Non-user	2.207(1.235-3.944)	
Hematological Comorbidity	No	1	0.018
	Yes	4.851(1.306-18.027)	
Renal Comorbidity	No	1	0.002
	Yes	3.039(1.525-6.057)	

Discussion

Worldwide considerable interventions and attempts were made to avoid subsequent hip fractures among the geriatric population. The chances of a second hip fracture are 1.1% in the first year following the first hip fracture, and the overall incidence was 6.0%. Various studies have been published to support the compliance of osteoporosis treatment and the associated risk of fragility fracture^{16,17}. However, there have been very few publications that demonstrate the significant contribution of bisphosphonate in avoiding subsequent hip fractures in South Asia. In a study conducted by Y-K et al. with their colleagues, about 8.6% of patients were affected by subsequent hip fracture; among them, 4.2% were compliant users, and 10.9% were non-user³. Our study found that compliant use of bisphosphonates reduced the risk of second hip fracture, which was found to be 3.5% in compliant users. However, this is the first retrospective analysis in Pakistan that assessed the relationship between compliant use of bisphosphonate and incidence of second hip fracture.

In the western world, many interventions were done to avoid subsequent fragility hip fractures among the geriatric population. Among these efforts, postoperative fracture assistant services have done the most appreciable work in reducing the risk of subsequent fractures^{14,18-21}. Bisphosphonates are now successfully used to prevent fractures; poor compliance with bisphosphonate treatment is the major limiting factor in the prevention of osteoporotic fracture^{22,23}. In our study, 64.6% of patients were non-compliant user of bisphosphonate after initial

hip fractures, which are nearly close to the reported data by Soong et al. was about 74.5%¹⁴. Multiple factors have an immense impact on the adherence of bisphosphonates. Especially in our region, lack of education and awareness on subsequent hip fractures still prevails^{24,25}.

Lack of motivational encouragement and poor socioeconomic status are other factors influencing the lower adherence to bisphosphonates use. Drug-related factors like gastro-esophageal reflux, post-infusion syndrome, and method ingestion might be the reason for lower compliance^{22,26-28}. Several measures must be taken to control such factors as a logistic patient coordination system, educational awareness protocol programs, earlier diagnosis, and proper treatment of osteoporosis to help prevent subsequent hip fractures among the geriatric population^{18,29,30}. In western society, orthopedics community health service lines have been established to decrease the risk of following fractures^{20,29}. However, this system is yet to be introduced in South Asia. Our study results highlighted the importance of the compliant user of bisphosphonates were at lower risk of developing a subsequent hip fracture simultaneously advanced age at the first hip fracture and lower bone mineral density have been correlated with increased risk of fracture. Hematological and renal comorbidities were diagnosed as an independent risk factors for second hip fracture, and similar factors were identified by YK et al. and Perez-Saez^{3,31}.

Our study had several limitations. First, all patients with osteoporosis-related second hip fractures were not coded in the nationwide database registry

because no such database exists in our country. Second, our study was retrospective, not prospective. Third, it was a single-center study, and a multicentric database will highlight other factors that influence the lower adherence to bisphosphonate use and help us create a nationwide database registry. Despite several confines, the results of our study consistently illustrate that compliant bisphosphonate consumption is related to a lower risk of a second or subsequent hip fracture.

Conclusion

The compliant use of bisphosphonates (Ibandronic Acid) among the geriatric age group has a significant impact on the prevention of second or subsequent hip fractures, and this is need to be an emphasis in clinical practice as it will help minimize the burden of hip fractures in geriatric age group.

Conflicts of Interest

No conflict of interest.

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