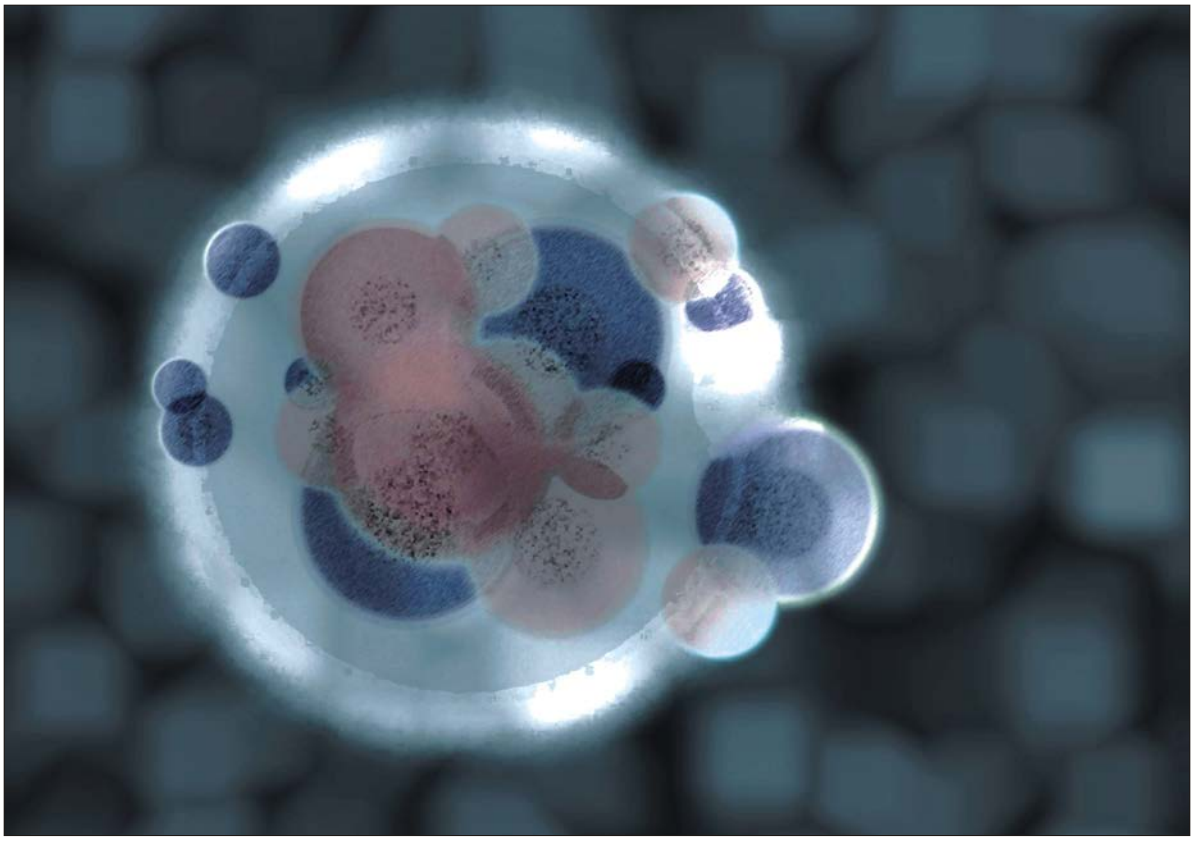

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The Use of Bisphosphonates by Postmenopausal Osteoporotic Women: Adherence and Side Effects

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Abstract: Adherence to bisphosphonates has become a major issue in clinical practice due to its effect on bone mineral density and fracture risk. This study aims to evaluate the adherence of a sample of postmenopausal osteoporotic women and to investigate the side effects experienced by them. For each participant in the study, a recent DXA scan (Dual-energy X-ray Absorptiometry) result confirming the diagnosis of osteoporosis was recorded. In addition, they were interviewed to fill the questionnaire and to answer six questions that comprised the modified Morisky scale. It was found that mean age of the medium or low adherence group (64.7 years) was significantly higher than mean age of the high adherence group (62.5 year), p = 0.029. Among women in the study, 73.6% of women were highly adherent. Adverse effects occurred in 26% of the sample. Family history of osteoporosis (odds ratio (OR): 0.453; confidence interval (CI): 0.228-0.899; p = 0.023) and tendency to fall (OR: 0.531; CI: 0.285-0.991; p = 0.047) were the two predictors for adherence to bisphosphonates. The adherence level reported in the current study was relatively high, this can be a good indicator about healthcare provided to postmenopausal osteoporotic women in the family practice clinic.

Key words: Adherence, osteoporotic, postmenopausal, women

INTRODUCTION

Bisphosphonates are considered a corner stone in the management of postmenopausal osteoporosis due to their ability to increase bone mineral density at the lumbar spine and hip and their capacity to reduce fracture risk (Rabenda *et al*., 2008). Bisphosphonates are found to reduce vertebral fracture risk by 30-65% (Delmas *et al*., 2005; Abella *et al*., 2011).

However, only one third to half of osteoporotic patients adhere to their medications as they are directed (Kothawala *et al*., 2007). Adherence to osteoporosis treatment is one of the important issues to control the disease worldwide and poor adherence is a major factor that leads to suboptimal clinical benefits (Rabenda *et al*., 2008). Poor adherence to bisphosphonates may lead to unwanted effects on bone mineral density and therefore, may increase fracture risk (Siris *et al*., 2006; Warriner and Curtis, 2009). Vertebral and hip fractures are primary reasons for major disability and reduction in quality of life and hip fractures lead to a twofold increase in mortality among women (Guilera *et al*., 2006).

In spite of the good safety record of bisphosphonates, they were associated with some serious adverse effects even with correct use (Abrahamsen, 2010). These adverse effects can lead in some cases to poor adherence to bisphosphonates therapy (Carr *et al*., 2006; Rossini *et al*., 2006). Factors that can affect or predict adherence to bisphosphonates include age, presence of fractures, type of drug, lack of motivation, family history of osteoporosis, family or personal history of fracture, tendency to fall and others (Papaioannou *et al*., 2003; Rossini *et al*., 2006; Abella *et al*., 2011).

This study aims to:

- Investigate adherence levels to bisphosphonates in postmenopausal osteoporotic women
- Determine the frequency of bisphosphonates adverse effects
- Investigate the predictors of adherence to bisphosphonates

MATERIALS AND METHODS

This is a cross sectional study, the study sample consisted of 288 postmenopausal osteoporotic women attending the family practice clinic at Jordan University Hospital in Amman – Jordan. The research was approved and funded by the Deanship of Academic Research in Jordan University. Informed consent was obtained from all study participants.

Inclusion criteria: Women who met the following inclusion criteria were included in the study: (1) Being

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older than 40 years, (2) Having primary menopause (Utian, 1994), (3) Diagnosed as having primary osteoporosis confirmed by a recent DXA scan (Dual-energy X-ray Absorptiometry) followed by the proper investigations to rule out secondary osteoporosis (Premaor and Compston, 2010) and (4) Have started their oral bisphosphonates (either alendronate or risedronate) at the time of diagnosis.

Osteoporosis has been defined on the basis of Bone Mineral Density (BMD) assessment. According to the WHO (World Health Organization) criteria, osteoporosis is defined as a BMD that lies 2.5 standard deviations or more below the average value for young healthy women (a T-score of <-2.5 SD) (WHO, 1994). BMD was measured by a Dual-energy X-ray Absorptiometry (DXA). Measurements were done at 2 sites: the lumbar spine (L1-L4) and the total hip. Measurement was carried out using Lunar iDXA.

Data collection: The family practice clinic in Jordan University Hospital involves 5 consultants, one specialist and 15 residents. From June 2011 to May 2012, a total of 288 women who fit to the inclusion criteria participated in the study after taking their verbal consent.

Each woman who participated in the study had a special form consisting of three parts. In the first part result of the DXA scan confirming osteoporosis diagnosis was documented. The second part consisted of a questionnaire that was filled for each woman by a trained research assistant who interviewed women, asked them about general aspects like age, weight, height, age at menopause and the adverse effects experienced by them due to the use of bisphosphonates. Body mass index was calculated from weight and height (WHO, 1998). The third part consisted of the six questions that comprised the modified Morisky scale (CMAG, 2006).

Data analysis: All data were entered to (SPSS 18, Chicago, USA software) statistical program.

Simple descriptive statistics were used through which results were expressed as percentages. Independent samples t-test and multiple logistic regression analysis were also used. A p value of <0.05 was used to reject the null hypothesis.

RESULTS

The study included a total of 288 postmenopausal osteoporotic women. Mean age±SD was 63.1±7.4 years, ages ranged from 43 to 90 years.

Table 1: General characteristics of the study sample by adherence levels according to the modified Morisky scale

	Adherence level (Mean±SD)		
Characteristic	High	Medium or low	p-value
Age	62.5±7.00	64.7±8.30	0.029
Weight	74.2±12.9	72.0±14.3	0.208
Height	156.2±6.50	155.3±11.4	0.435
BMI	30.5±5.50	30.3±8.30	0.805
Age of menopause	48.4±5.80	47.7±6.00	0.334
T-score at the lumbar spine	2.9±0.60	2.9±0.80	0.591
T-score at the total hip	2.3±0.80	2.2±0.7	0.344

SD: Standard deviation, BMI: Body mass index

Table 2: Adherence levels of the study sample according to the modified Morisky scale

Adherence	No.	Percentage
Low	34	11.8
Variable	42	14.6
High	212	73.6

Table 3: Frequencies of the different adverse effects of bisphosphonates reported by women in the study

Side effect	No.	Percentage
Gastrointestinal	57	19.8
Myalgia and arthralgia	8	2.8
Photophobia	5	1.7
Thigh pain	5	1.7
Total	75	26

From a total of 288 women

Table 1 shows the general characteristics of the study sample by adherence levels according to the modified Morisky scale. It was observed that the mean age of the medium or low adherence group (64.7 years) was significantly higher than mean age of the high adherence group (62.5 year), p = 0.029. Other characteristics were similar in both groups.

Table 2 shows the adherence levels of the study sample according to the modified Morisky scale. It was found that 73.6% of women were highly adherent to bisphosphonates with low or variable adherence occurring in 26.4% (sum of 11.8% low and 14.6% variable adherence levels) of women.

Table 3 shows the frequencies of the different adverse effects of bisphosphonates reported by women in the study. Adverse effects occurred in 26% of women. With the most frequent one being gastrointestinal discomfort (19.8%), followed by myalgia and arthralgia (2.8%), photophobia (1.7%) and thigh pain (1.7%).

Table 4 shows the binary logistic regression analysis and odds ratio with 95% Confidence Interval to predict adherence according to the modified Morisky scale. Family history of osteoporosis (OR:0.453; CI: 0.228-0.899; p = 0.023) and tendency to fall (OR: 0.531; CI: 0.285-0.991; p = 0.047) were the two predictors for adherence to bisphosphonates.

Table 4: Binary logistic regression analysis and odds ratio with 95% confidence interval to predict adherence according to the modified Morisky scale

Factor	OR	95%	CI	p
Marital status	1.126	0.832	1.523	0.442
Education	0.972	0.717	1.316	0.853
Occupation	1.446	0.775	2.699	0.246
Diabetes	0.702	0.39	1.265	0.239
Hypertension	1.084	0.602	1.952	0.788
Age at menarche	1.073	0.918	1.255	0.375
Age at menopause	0.973	0.927	1.021	0.261
Smoking	0.607	0.24	1.535	0.292
Coffee intake	0.923	0.497	1.715	0.8
Milk intake	1.562	0.754	3.233	0.23
Family history of osteoporosis	0.453	0.228	0.899	0.023
Family history of fractures	1.406	0.518	3.816	0.504
Personal history of fractures	1.798	0.858	3.767	0.12
Tendency to fall	0.531	0.285	0.991	0.047
Generalized body pain	0.915	0.493	1.697	0.778

OR: Odds ratio, CI: Confidence interval

DISCUSSION

Adherence to osteoporosis medications has become a major issue in the management of postmenopausal osteoporosis in clinical practice due to its effect on bone mineral density status and fracture risk. This study aims to evaluate the adherence of a sample of postmenopausal osteoporotic women to bisphosphonates therapy according to the modified Morisky scale.

The mean age of the patient's group with medium or low adherence (64.7 years) was significantly higher than the mean age of the high adherence group (62.5 years), p = 0.029. Cadarette *et al.* (2011) have reported a similar result, although the difference in their study did not reach a statistically significant level. On the other hand, Papaioannou *et al.* (2003) have reported a contrary finding, as they indicated that increased age was associated with greater adherence. In the study of Carr *et al.* (2006), ages of the adherent and non adherent groups were the same. Results from the current study of higher age of the group with medium or low adherence might be explained by the decline in organizational skills with advancing age, which might be an obstacle for taking the medications properly by older patients.

The frequency of highly adherent patients reported in the current study is higher than what has been reported in a number of studies (Diez *et al.*, 2012; Cadarette *et al.*, 2011; Downey *et al.*, 2006). Different results from different studies may vary due to the variant methods used to measure adherence. Some studies utilize the Morisky Green test, others may use the medication possession ratio or others (Rabenda *et al.*, 2008; Cadarette *et al.*, 2011; Abella *et al.*, 2011). A possible explanation for the relatively high level of adherence in the current study might be that all patients are insured, which prevents the cost of the drug to be a reason for not taking the medication. Another important reason might be the adoption of a patient centered approach by family physicians, which involves the patient in taking responsibility of his/her disease, leading to improved compliance.

A number of bisphosphonates adverse effects have been reported in the currents study (26%). The most frequent adverse effect was gastrointestinal discomfort occurring in 19.8% of the patients. Similar to these results, Rossini *et al.* (2006), reported that adverse effects occurred in around 25% of their study sample and Aki *et al.* (2003) have found that 20.8% of their study sample suffered gastrointestinal side effects. Reviews by Abrahamsen (2010) and Pazianas and Abrahamsen (2011) have reported that upper gastrointestinal adverse effects are the most important reason given by patients for not continuing their treatment. Rossini *et al.* (2006) and others have reported that patients who suffered from gastrointestinal adverse effects in their study had poor compliance (Penning-van Beest *et al.*, 2006). It is suggested that poor adherence due to upper gastrointestinal side effects might be overcome by providing adequate explanation of the DXA results to the patients, assuming that when patients understand their bone densitometry results they tend to follow their treatment regimen better (Pickney and Arnason, 2005; Rossini *et al.*, 2006; Pazianas and Abrahamsen, 2011). Moreover, listening to the patient adequately and offering solutions to overcome the discomfort caused by bisphosphonates might result in better adherence outcomes.

Family history of osteoporosis was found to be one of the predictors for adherence to bisphosphonates therapy in the current study. Abella *et al.* (2011) have reported the same finding. Additionally, Lau *et al.* (2008) have reported that patients with a family history of osteoporosis were motivated more than others to adhere to their treatment. It seems that family history of osteoporosis represents a motivation for patients to adhere to their medications due to the better knowledge they gained about the disease through their family member's experience.

Tendency to fall was found to be another predictor for bisphosphonates adherence in the current study. The same finding was reported by Abella *et al.* (2011). Patients who tend to fall might have the fear from fractures more than others, this might have motivated them to adhere to their treatment in order to protect themselves from fractures and their complications.

This study has the following limitations: First, the researchers did not assess the exact reasons for discontinuing the treatment, this prevented us from

establishing a specific correlation between the side effects and non adherence. Second, the modified Morisky scale is considered a measure of self reported adherence, it would have been useful if more precise measures in addition were utilized. Third, the study was conducted in a single family practice clinic in Jordan, it would be better if it can be repeated in other family practice and different specialty clinics to be able to generalize the results on all postmenopausal osteoporotic women in Jordan.

CONCLUSION

The adherence level reported in the current study was relatively high, this can be a good indicator about healthcare provided to postmenopausal osteoporotic women in the family practice clinic. Emphasizing on patient centered care and good doctor patient relationship and communication in terms of providing adequate education about osteoporosis is vital in this regard to empower the patients to be responsible of their disease seeking better clinical and therapeutic outcomes.

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