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ORIGINAL ARTICLE

Assessment of patient-reported outcomes (PROs): treatment satisfaction, medication adherence, and quality of life (QoL) and the associated factors in postmenopausal osteoporosis (PMO) patients in Korea

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Abstract

Patient-reported outcomes (PROs) provide practical guides for treatment; however, studies that have evaluated PROs of women in Korea with postmenopausal osteoporosis (PMO) are lacking. This cross-sectional, multi-center (29 nationwide hospitals) study, performed from March 2013 to July 2014, aimed to assess PROs related to treatment satisfaction, medication adherence, and quality of life (QoL) in Korean PMO women using osteoporosis medication for prevention/treatment. Patient demographics, clinical characteristics, treatment patterns, PROs, and experience using medication were collected. The 14-item Treatment Satisfaction Questionnaire for Medication (TSQM) (score-range, 0–100; domains: effectiveness, side effects, convenience, global satisfaction), Osteoporosis-Specific Morisky Medication Adherence Scale (OS-MMAS) (score-range, 0–8), and EuroQol-5 dimensions questionnaire (index score range, −0.22 to 1.0; EuroQol visual analog scale score range, 0–100) were used. To investigate factors associated with PROs, linear (treatment satisfaction/QoL) or logistic (medication adherence) regression analyses were conducted. A total of 1804 patients (age, 62 years) were investigated; 60.1% used bisphosphonate, with the majority (67.2%) using weekly medication, 27.8% used daily hormone replacement therapy, and 12.1% used daily selective estrogen receptor modulator. Several patients reported gastrointestinal (GI) events (31.6%) and dental visits due to problems (24.1%) while using medication. Factors associated with the highest OS-MMAS domain scores were convenience and global satisfaction. GI events were associated with non-adherence. TSQM scores for effectiveness, side effects, and GI risk factors were significantly associated with QoL. Our study elaborately assessed the factors associated with PROs of Korean PMO women. Based on our findings, appropriate treatment-related adjustments such as frequency/choice of medications and GI risk management may improve PROs.

Keywords Postmenopausal osteoporosis · Treatment satisfaction · Medication adherence · Quality of life · Gastrointestinal events

Introduction

Postmenopausal osteoporosis (PMO) constitutes up to 80% of all types of osteoporosis [1]. In 2012, approximately one-third of women aged 50 years or older in Korea reported having osteoporosis [2]. Decreased bone mass and estrogen levels in PMO increase the risk of bone fractures [3, 4]. Osteoporotic fractures represent a serious health problem

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that leads to disability and increased mortality risk [5]. The crude mortality rate of hip fractures alone can be as high as 16.2% at 1-year post-injury for those with PMO [6].

Several drugs are available for PMO [1, 7], but the most commonly used agents are bisphosphonates (BPPs) [8]. Despite their well-proven efficacy, because of their poor absorption, they are accompanied by frequent gastrointestinal (GI) side effects and complex dosing requirements [9]. Furthermore, BPPs are known to increase the risk of osteonecrosis of the jaw (ONJ) in some patients [10]. Hormone replacement therapy (HRT) is also a valuable option because it can relieve postmenopausal vasomotor symptoms; however, there have been controversial reports of associated increased risks of breast cancer and cardiovascular disease (CVD). Another available agent is the selective estrogen receptor modulator (SERM). Compared to BPP, higher treatment satisfaction and quality of life (QoL) were observed for patients using SERM, although unresolved concerns regarding CVD risks remain [11, 12].

Patient-reported outcomes (PROs) refer to measurements of any health status aspect directly indicated by the patient [13]. These are important because they are often associated with overall treatment efficacy and are often inter-related [14]. Approximately, half of the patients who make incorrect treatment-related decisions and become "non-adherent" report low treatment satisfaction [15, 16]. With osteoporosis, substantial QoL debilitation is often observed in these patients [17]. It has been reported that after osteoporotic hip fracture, 75% of individuals cannot return to their activities of daily living, mostly due to their inability to walk [18].

Factors associated with PROs of osteoporosis include side effects during treatment [19]. Of these, GI events for those with PMO require more attention because these patients are elderly and are at higher risk for GI events. Furthermore, GI events have been associated with low treatment satisfaction, medication discontinuation, and poor QoL [7]. Patients using osteoporotic medication frequently report GI events, which are experienced by up to 52% of osteoporosis patients [20].

Due to the aging society, the prevalence of PMO is increasing; however, PRO studies of PMO are scarce in Korea. Therefore, in this study, we primarily figured out the adherence and investigated factors, including GI-specific factors, associated with medication adherence. We also figured out the treatment satisfaction and QoL and identified related factors with satisfaction and QoL, of Korean PMO women using osteoporotic medications. Findings from this study will provide valuable perspectives that could help to create strategic approaches for the management of PMO.

Materials and methods

Study population

This was a cross-sectional, multi-centered, observational study conducted at 29 nationwide tertiary hospitals in the divisions of endocrinology, orthopedic surgery, and obstetrics and gynecology in South Korea. The study period was from March 2013 to July 2014. To collect generalizable data, we estimated the target sample size based on the assumption that the medication adherence (p) of PMO patients is 48% [21]. With a significance level of 0.05 ($Z = 1.965$; confidence interval, 95%) and an estimated error rate (D) of 2.3%, the required number of enrolled patients according to the following equation was calculated as approximately 1800:

$$N = Z^2 \times p(1-p)/D^2.$$

Postmenopausal patients who had used oral medications for the purpose of osteoporosis prevention or treatment for at least 1 month to a maximum 12 months for the first time were included. Patients were excluded if they had started using medication less than 1 month prior to enrollment or if they were using only vitamin D or calcium for the purpose of osteoporosis prevention or treatment. Patients were informed about the purpose of the study, and written informed consent was obtained. This study was approved by the Institutional Review Board of all participating hospitals. All patients provided their informed consent prior to their enrollment in the study.

Data collection

Patients were enrolled during their regular visits if they met all of the inclusion criteria for this study. Data were collected via chart reviews and patient surveys. Four main variables were collected: 1) demographics and clinical characteristics including age, body mass index (BMI), PMO medication duration, bone mineral density (BMD, femoral neck, total hip and lumbar spine L2–L4), history of osteoporotic fracture, family history of osteoporosis, comorbidities (such as hypertension, dyslipidemia, thyroid disease, diabetes mellitus, cancer, and arthritis), number of GI risk factors (GI comorbidities including gastritis, gastroesophageal reflux disease, dyspepsia, GI ulcer, and gastric perforation), current smoking, alcohol consumption, current use of aspirin, non-steroidal anti-inflammatory drugs, anti-coagulants, or steroids; specially, BMD is related with osteoporosis diagnosis. PMO diagnostic criteria in Korea are as follows; (1) at least 1 year after menopause, (2) femoral neck or total hip or lumbar spine L2–L4: T-score below − 2.5, (3) patients using medication for at least 1–12 months. Using these diagnostic criteria, patients were classified as normal, osteopenia and osteoporosis. 2) Experience during PMO medication

use, such as history/type of GI events (including heartburn, dyspepsia, nausea, and vomiting) and history/purpose of dental visits (planned dental visits within 3 months were also included); 3) treatment patterns such as type of PMO medication (BPP, SERM, HRT), medication frequency (i.e., daily, weekly, monthly), use of GI protectants, and non-osteoporotic medications; and 4) PROs such as treatment satisfaction, medication adherence, and QoL.

PROs

Treatment satisfaction was measured using the 14-item Treatment Satisfaction Questionnaire for Medication (TSQM) questionnaire, which provides satisfaction scores for each of the following four domains: effectiveness, side effects, convenience, and global satisfaction. The scores for each TSQM domain range from 0 to 100, and higher scores indicate better satisfaction [22].

Medication adherence was measured by the Osteoporosis-Specific Morisky Medication Adherence Scale (OS-MMAS). The OS-MMAS scores range from 0 to 8, with higher scores indicating better adherence. Patients were categorized into the following groups: low adherence (score < 6), medium adherence (score ≥ 6 but < 8), and high adherence (score ≥ 8) [23].

General health-related QoL and osteoporosis-specific QoL were measured by the European Quality of Life–5 Dimensions (EQ-5D-3L) questionnaire. QoL scores from the EQ-5D Index (score range, − 0.229 to 1.0) and EuroQol visual analog scale (EQ VAS; score range, 0–100) were evaluated, and higher scores indicated better QoL [24]. The EQ-5D-3L descriptive system consists of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension consists of three levels: no problems, some problems, and severe problems [25].

Statistical analysis

Patient demographics and clinical characteristics, experiences during treatment, treatment patterns, number of GI risk factors, and PRO scores were summarized as the number of patients (percentage) for categorical variables or mean ± standard deviation (SD) for continuous variables. To examine the association between the aforementioned variables and PROs, univariable analysis was conducted using the Chi-square test for categorical variables and the Student *t* test for continuous variables.

To analyze factors associated with treatment satisfaction (TSQM domains: effectiveness, side effects, convenience, and global satisfaction) and QoL (EQ-5D Index, EQ-VAS), a multiple linear regression model was used. For medication adherence, logistic regression analysis was used. During this analysis, patients in the high adherence (OS-MMAS score, 8) group were included in the adherence group; patients in the low and medium adherence (OS-MMAS score < 8) groups were included in the non-adherence group [26]. Age, BMI, PROs, and other variables with a p value < 0.1 according to the univariable analysis were included in the model. In our analyses, patients who had taken monotherapy only were included. Patients who used more than one medication in their PMO prophylaxis/treatment were not included in the analyses.

All statistical analyses were performed using PASW Statistics version 20.0 (SPSS Inc, Chicago, IL, USA), and all p values obtained from statistical analyses were the results of two-sided tests for which the statistical significance level was set at $p < 0.05$.

Results

Patient characteristics

A total of 1804 postmenopausal women using osteoporosis medication (mean age, 62 years; mean duration of medication, 161 days) participated in this study. A total of 65.7% had osteoporosis at the time of study enrollment. The remaining patients had osteopenia (23.2%) or normal BMD (11.1%). Approximately, 30% of patients had a history of bone fracture; hip fracture (13.3%) was the most common. A total of 16% of patients had a family history of osteoporosis. Most patients had comorbidities (61.8%) such as hypertension, which was the most prevalent (31.4%). The GI risk factor assessment showed fewer than one GI risk factor per patient, on average. The most prevalent GI risk factor was alcohol consumption (24.6%), and 31.6% of the patients had experienced GI events while using PMO medication. Heartburn was the most common type of GI event; it occurred in approximately 17% of patients. Approximately, 24% patients also had a history of dental visits or planned dental visits related to problems associated with medication (Table 1).

Treatment patterns

The most commonly used PMO medication was BPP (59.7), followed by HRT (27.7%) and SERM (12.6%). Most patients were using daily (49.6%) or weekly (40.6%) medications (Table 2). Approximately, 70% of BPP use was weekly, whereas 100% of SERM and HRT use was daily (Fig. 1). A total of 14% of patients were using GI protectants (Fig. 1).

PROs

Treatment satisfaction scores for the global satisfaction domain were the lowest among all four domains (mean ± SD: 53.8 ± 15.3), followed by effectiveness (56.1 ± 11.8),

Table 1 Patient characteristics

Variables	$n=1804$	%
Age (years), mean ± SD	62.33 ± 10.90	
BMI (kg/m^2), mean ± SD	22.94 ± 3.12	
PMO medication duration (days), mean ± SD	161.11 ± 103.28	
BMD	$n=1683$	
Osteoporosis	1105	65.7
Osteopenia	391	23.2
Normal	187	11.1
Patient history of osteoporotic fracture[a]	524	29.0
Hip	240	13.3
Vertebral	125	6.9
Wrist	76	4.2
Family history of osteoporosis	289	16.0
Comorbidities[a]	1114	61.8
Hypertension	566	31.4
Dyslipidemia	297	16.5
Thyroid disease	282	15.6
Diabetes mellitus	263	14.6
Cancer	208	11.5
Arthritis	148	8.2
Number of GI risk factors[a], mean SD (min, max)	0.61 ± 0.77 (0, 5)	
Alcohol consumption	282	15.6
Aspirin	214	11.9
GI comorbidities[b]	305	16.9
NSAIDs	150	8.3
Smoker	66	3.7
Anticoagulants	46	2.5
Steroids	41	2.3
GI events[a]	570	31.6
Heartburn	302	16.7
Dyspepsia	267	14.8
Nausea	186	10.3
Vomit	35	1.9
Dental visits[a]	435	24.1
Tooth-implant	141	7.8
Cavity	139	7.7
Periodontal disease	103	5.7
Dentures	77	4.3

[a]A multiple response item

[b]Gastritis, gastroesophageal reflux disease, dyspepsia, upper GI ulcer, and gastric perforation

Table 2 Treatment patterns

Variables	*N*	%
PMO medication	$n=1792$	
BPP	1069	59.7
HRT	497	27.7
SERM	226	12.6
PMO medication frequency	$n=1790$	
Daily	888	49.6
Weekly	726	40.6
Monthly	176	9.8
Use of GI protectants	252	14.0
Use of non-osteoporotic medications	1261	70.0

convenience (63.0 ± 12.7), and side effects (64.2 ± 22.5) (Fig. 2a). The proportion of those with high adherence to medication (OS-MMAS score = 8) was the lowest (27.4%), whereas the proportion with medium adherence to medication (OS-MMAS score, ≥ 6 but < 8) (42.2%) was the highest (Fig. 2b). The proportion of patients with some or severe problems with each QoL dimension was highest for pain/discomfort (45.0%), followed by anxiety/depression (37.0%), usual activity (28.5%), mobility (27.2%), and self-care (16.7%) (Table 3). The mean QoL scores were 0.71 ± 0.18 (EQ-5D Index) and 69.20 ± 17 (EQ-VAS) (Fig. 2c).

Factors associated with treatment satisfaction

As a result of multivariable analysis, none of the factors was significantly associated with all four TSQM domains simultaneously. Use of HRT compared to BPP was positively associated with effectiveness ($B=7.541$; $p<0.001$), convenience ($B=7.154$; $p<0.001$), and global satisfaction ($B=8.486$; $p<0.001$) domains. The two factors that were negatively associated with these three domains were GI events (effectiveness: $B=-2.358$ and $p<0.001$; convenience: $B=-2.669$ and $p<0.001$; global satisfaction: $B=-2.862$ and $p<0.001$) and dental visits (effectiveness: $B=-1.863$ and $p=0.004$; convenience: $B=-1.866$ and $p=0.007$; global satisfaction: $B=-2.156$ and $p=0.013$) (Table 4).

Factors associated with medication adherence

Treatment convenience was significantly associated with medication adherence (adjusted odds ratio [OR] = 1.034; $p<0.001$). Duration of medication use (OR 0.998; $p=0.002$), family history (OR 0.607; $p=0.007$), GI events (OR 0.666; $p=0.007$), use of HRT (OR 0.380; $p=0.004$) compared to BPP, and daily use (OR 0.485; $p=0.008$) or weekly use (OR 0.367, $p<0.001$) compared to monthly use of medication were associated with non-adherence (Table 4).

Factors associated with QoL

Satisfaction with effectiveness (EQ-5D Index: $B=0.002$; $p=0.030$) and satisfaction with side effects (EQ VAS: $B=0.105$, $p=0.021$) were positively associated with QoL. Age (EQ-5D Index: $B=-0.007$ and $p<0.001$; EQ VAS:

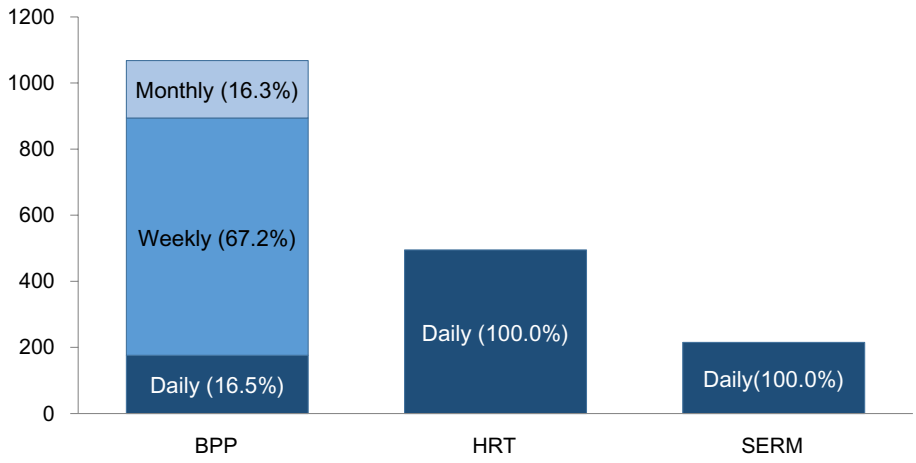

Fig. 1 Osteoporotic treatment pattern and medication frequency. BPP ($n=1068$), HRT ($n=495$), SERM ($n=215$) patients who did not answer the frequency of their PMO medication were excluded from the figure

$B=-0.336$ and $p=0.006$) and increased number of GI risk factors (EQ-5D Index: $B=-0.043$; $p=0.004$) were negatively associated with QoL (Table 4).

Discussion

PROs reveal patients' perspectives and can help providers to understand the progression of disease and treatment outcomes [13]. Furthermore, they allow sensitive detection of physical and psychological problems that patients experience in real-world treatment settings which otherwise may have been overlooked [27]. Therefore, PROs have become an important treatment evaluation tool over the years, especially for the management of chronic diseases that often require long-term management. To the best of our knowledge, this was the first attempt to analyze the factors associated with treatment satisfaction, medication adherence, and QoL in one study of Korean PMO women. Our study was unique because it also assessed GI-specific factors and their effects on the aforementioned PROs.

In this study, higher treatment satisfaction was observed for non-BPP users. Such results were also reported in other previous studies. In a PRO study conducted in Asia, raloxifene users reported higher treatment satisfaction, and the proportions of patients responding in each of the three response categories ("satisfied", "no opinion", and "dissatisfied") were 71.4, 21.2, and 7.4%, respectively, for raloxifene and 59.2, 21.7, and 19.1%, for BPP, respectively [11, 28]. This may be due to more convenient dosing and fewer GI problems [10, 11, 29]. This study highlighted the importance of GI risk management during PMO treatment. It was found that less experience with GI events and the use of GI protectants significantly increased treatment satisfaction.

For the first time, we reported the association of dental visits with treatment satisfaction regarding PMO management. Decreased bone mass with osteoporosis is associated with a higher risk of dental health problems. For every 1% decrease in BMD per year, the risk of tooth loss increases more than four times [30]. Additionally, regular dental visits are recommended for BPP users because these patients are at risk for ONJ development [10]. Although the causality between the dental visits and the treatment patterns per se was not analyzed, our study results showed that these visits may decrease treatment satisfaction. Therefore, dental health management should not be overlooked during PMO treatment.

Results of this study showed that less than 30% of patients practiced high medication adherence. Despite many reports of the clear association between medication adherence and treatment outcomes for osteoporosis, suboptimal adherence is often reported for patients using osteoporosis medication; overall adherence to osteoporosis therapies is known to range from 40 to 70% [31]. Medication adherence is pivotal for eliciting the clinical benefits of osteoporosis treatment. In a different study, increased BMD of the lumbar spine was significantly higher in patients who had used at least two-thirds of the prescribed doses (3.8%) compared to those who used less than two-thirds (2.1%) [32]. Our study showed that to increase medication adherence, it is necessary to maximize treatment convenience and reduce treatment duration, GI events, or medication frequency. Use of HRT and family history of osteoporosis were also associated with low medication adherence (OS-MMAS score <8). This may be because patients using HRT are doing so for prevention rather than treatment. The relationship between family history and medication adherence remains controversial [33–35].

In this study, the EQ-5D Index of PMO patients was 0.71 ± 0.18, which is comparable to the QoL results of osteoporotic women reported by a previous study performed in Korea (0.71 ± 0.18 vs. 0.799 ± 0.190) [36]. Our results revealed that the most affected QoL dimension of PMO patients was pain/discomfort (45.0%). This observation

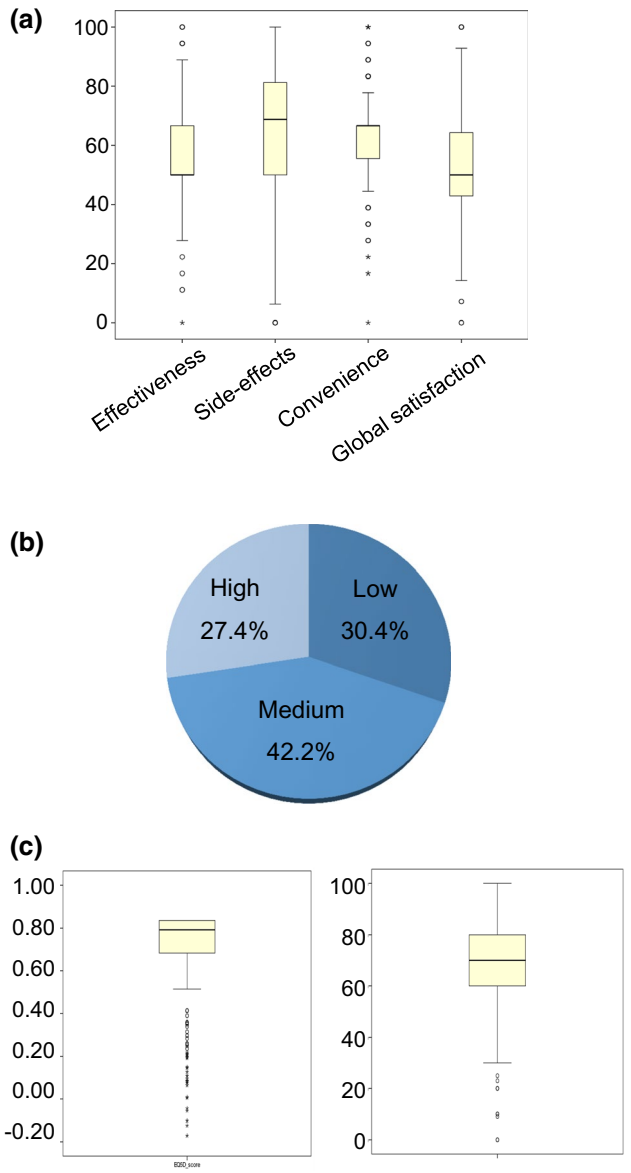

Fig. 2 PROs ($n=1804$). **a** Treatment satisfaction. TSQM scores (mean ± SD) for each domain (from left) effectiveness 56.09 ± 11.81, side effects 64.15 ± 22.46, convenience 63.03 ± 12.67, and global satisfaction 53.79 ± 15.31. **b** Medication adherence. Proportion of patients (%) in high-, medium-, and low-adherence group. **c** QoL. EQ-5D Index; 0.71 ± 0.18 (left), EQ VAS; 69.20 ± 17.1 (right)

Table 3 Patients in each level of QoL dimensions ($n=1804$)

n (%)	No problem	Some problem	Severe problem
Mobility	1313 (72.8)	480 (26.6)	11 (0.6)
Self-care	1502 (83.3)	275 (15.2)	27 (1.5)
Usual activity	1290 (71.5)	485 (26.9)	29 (1.6)
Pain/discomfort	992 (55.0)	766 (42.5)	46 (2.5)
Anxiety/depression	1136 (63.0)	647 (35.9)	21 (1.2)

was also consistent with the results of osteoporosis patients reported by a different study [37].

Our study revealed the importance of GI-specific factors in PMO treatment. GI events during PMO medication use were significantly associated with worse treatment satisfaction and medication adherence. Additionally, use of GI protectants significantly increased treatment satisfaction, whereas GI risk factors for PMO patients significantly decreased QoL. Our study found that a significant number of patients experienced GI events during PMO medication use (32%). Therefore, the importance of preventing GI events and managing GI risk should be further emphasized with PMO treatment.

In this study, proportion of patients at GI risk (i.e., those who had at least one of the GI risk factors defined in this study) were highest for BPP (59.8%), followed by HRT (27.8%) and SERM (13.4%). BPPs have shown to effectively increase BMD and reduce vertebral as well as non-vertebral fractures risk by as much as 40 and 30%, respectively [38]. Despite its well-proven efficacy, oral BPPs may cause upper GI side effects such as esophagitis and myalgias and are contraindicated in patients with certain comorbidity of the upper GI tract [39]. Therefore, for patients at higher GI risk, alternative medications such as HRT and SERMS, denosumab, other than BPP, or other routes of administration (such as intravenous BPP) or less frequent administrations could be considered [40, 41].

According to previous PMO studies, compliance was highest in BPP and lowest in HRT. The monthly/daily frequency of BPP was an important factor in compliance, being highest for monthly preparations and lowest for daily regimens [42]. The compliance of the previous foreign study was much better than that of Korea. The fact that Korea uses more daily BPP and less monthly BPP than foreign country may have affected.

Despite the convenience of frequency, in other study, the satisfaction of BPP was lower than that of SERM [28]. This tendency is consistent with our study. Therefore, we considered the factors such as the GI event of the BPP [7], and we described the more accurate Korea treatment pattern. Another well-known factor for treatment satisfaction and medication adherence is the treatment failure (i.e., the occurrence of fractures). In our study, patient history of osteoporotic fracture was adjusted in our regression analyses only if they had p value of ≤ 0.1 in the univariable analyses. As a result, history of fracture was only adjusted for regression analyses on treatment satisfaction; effectiveness/convenience, medication adherence and QoL. History of fracture was not a significant factor for treatment satisfaction on side effects/global satisfaction.

This study was a large-scale observational study that included approximately 1800 patients with PMO from Korean medical institutions; therefore, it provided

Table 4 Factors associated with treatment satisfaction, medication adherence and QoL ($n=1792$)

Variable (reference)	Treatment satisfaction								Medication adherence		QoL			
	Effectiveness		Side effects		Convenience		Global satisfaction		OR (95% CI)	*p*	EQ-5D Index		EQ VAS	
	B	*p*	*B*	*p*	*B*	*p*	*B*	*p*			*B*	*p*	*B*	*p*
Age	0.047	0.154	0.023	0.876	−1.121	0.000	0.074	0.073	1.010 (0.995–1.025)	0.201	−0.007	0.000	−0.336	0.006
BMI			0.377	0.362										
Treatment duration	0.007	0.006					0.011	0.002	0.998 (0.997–0.999)	0.002	0.000	0.280	0.000	0.975
Osteopenia (normal)	2.251	0.040	−5.033	0.255	1.401	0.229	1.684	0.248	1.106 (0.648–1.886)	0.712	0.064	0.077	−0.418	0.901
Osteoporosis (normal)	1.410	0.260	−7.705	0.129	3.215	0.016	0.963	0.564	0.871 (0.472–1.606)	0.657	0.038	0.373	1.307	0.734
History of fracture	−0.321	0.628			0.080	0.909			1.109 (0.822–1.495)	0.498	−0.043	0.081	−2.518	0.288
Family history									0.607 (0.424–0.870)	0.007	0.029	0.223		
Comorbidities	−1.000	0.128			−1.145	0.101	−1.585	0.047			0.025	0.276	−0.145	0.946
Number of GI RFs	−0.486	0.187			−0.335	0.392			0.962 (0.808–1.146)	0.666	−0.043	0.004	−1.498	0.254
GI events	−2.358	0.000			−2.669	0.000	−2.862	0.000	0.666 (0.496–0.896)	0.007	−0.039	0.074	−3.401	0.101
Dental visits	−1.863	0.004	0.677	0.808	−1.866	0.007	−2.156	0.013	0.776 (0.566–1.065)	0.116				
Treatment patterns														
SERM (BPP)	1.084	0.349	−0.543	0.932	5.501	0.000	6.739	0.000	0.732 (0.429–1.249)	0.252	−0.023	0.671	−2.965	0.535
HRT (BPP)	7.541	0.000	−1.329	0.825	7.154	0.000	8.486	0.000	0.380 (0.198–0.730)	0.004	−0.038	0.489	−6.891	0.134
Weekly (monthly)	0.058	0.952	10.466	0.004	−1.402	0.172	1.199	0.348	0.367 (0.242–0.556)	0.000	0.038	0.185	−1.247	0.645
Daily (monthly)	−0.040	0.974	7.870	0.144	−1.744	0.177	−1.956	0.225	0.485 (0.284–0.829)	0.008	0.047	0.323	2.266	0.573
GI protectants							2.680	0.014			0.021	0.495	−2.646	0.352
Other medication	−0.063	0.928			−0.550	0.462					0.001	0.957	−0.459	0.842
PROs														
Medication adherence	2.622	0.000			5.167	0.000			–		0.038	0.128	4.322	0.069
Treatment satisfaction														
Effectiveness	–		–		–		–		1.009 (0.995–1.024)	0.220	0.002	0.030	−0.014	0.886
Side effects	–		–		–		–				0.000	0.452	0.105	0.021
Convenience	–		–		–		–		1.034 (1.022–1.046)	0.000	0.001	0.399	0.114	0.143
Global satisfaction	–		–		–		–		1.004 (0.993–1.016)	0.458	0.000	1.000	0.125	0.131

epidemiological data representative of the Korean PMO population. The results of this study can be used to help understand the characteristics and treatment patterns in a real-world hospital setting in Korea. Furthermore, because patients in this study had a relatively short duration of PMO medication use (less than 6 months), our results can be applied to create treatment strategies for long-term disease management because it disclosed factors associated with PROs during the earlier phase of medication use.

There were some limitations to this study. First, frequency of medication use was uneven, with more than half of BPP treatments used weekly and all HRT and SERM treatments used daily. However, this limitation was managed by adjusting the type of medication in our multivariable analysis. Second, due to the cross-sectional study design, a causal relationship between the variables and the PROs could not be analyzed. Third, patients who participated in the surveys tended to be healthier, more motivated, and more likely to be compliant than the general population, which may have limited the generalizability of these results.

Despite these limitations, our findings elaborately assessed the status and factors associated with PROs of Korean PMO women. The frequency of medications used was BPP, HRT and SERM in that order. Factors associated with the highest adherence scores were convenience and global satisfaction. GI events were negatively associated with adherence score. Treatment effectiveness, side effects and GI risk factors were also associated with QoL.

The findings revealed that considerable proportion of patients experience GI events during PMO medication use and implied significant effect of GI risk management on PROs. Furthermore, for the first time, we report the negative association between dental visits during medication with patient's treatment effectiveness, convenience and global satisfaction. Based on our findings, appropriate treatment-related adjustments, such as frequency and choice of medications, and concomitant use of GI protectants may resolve these issues. These findings will help contribute to creating an effective treatment strategy that will improve PROs of PMO women in Korea.

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Compliance with ethical standards

Statement of human and animal rights All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest All authors have no conflicts of interest.

References

1. Baccaro LF, Conde DM, Costa-Paiva L, Pinto-Neto AM (2015) The epidemiology and management of postmenopausal osteoporosis: a viewpoint from Brazil. Clin Interv Aging 10:583–591. https://doi.org/10.2147/CIA.S54614
2. Choi YJ, Oh HJ, Kim DJ, Lee Y, Chung YS (2012) The prevalence of osteoporosis in Korean adults aged 50 years or older and the higher diagnosis rates in women who were beneficiaries of a national screening program: the Korea National Health and Nutrition Examination Survey 2008–2009. J Bone Miner Res 27:1879–1886. https://doi.org/10.1002/jbmr.1635
3. Anonymous (1993) Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med 94:646–650
4. Wactawski-Wende J (2001) Periodontal diseases and osteoporosis: association and mechanisms. Ann Periodontol 6:197–208. https://doi.org/10.1902/annals.2001.6.1.197
5. Watts NB, Manson JE (2017) Osteoporosis and fracture risk evaluation and management: shared decision making in clinical practice. JAMA 317:253–254. https://doi.org/10.1001/jama.2016.19087
6. Yoon HK, Park C, Jang S, Jang S, Lee YK, Ha YC (2011) Incidence and mortality following hip fracture in Korea. J Korean Med Sci 26:1087–1092. https://doi.org/10.3346/jkms.2011.26.8.1087
7. Woo C, Gao G, Wade S, Hochberg MC (2010) Gastrointestinal side effects in postmenopausal women using osteoporosis therapy: 1-year findings in the POSSIBLE US study. Curr Med Res Opin 26:1003–1009. https://doi.org/10.1185/03007991003633603
8. Patrick ARBM, Losina E, Schousboe JT, Cadarette SM, Mogun H, Solomon DH (2010) The complex relation between bisphosphonate adherence and fracture reduction. J Clin Endocrinol Metab 95:3251–3259
9. Chapurlat R, Delmas PD (2004) Treatment of postmenopausal osteoporosis. Rev Prat (Traitement de l'osteoporose post-menopausique) 54:2120–2126
10. Hellstein JW, Adler RA, Edwards B, Jacobsen PL, Kalmar JR, Koka S, Migliorati CA, Ristic H, American Dental Association Council on Scientific Affairs Expert Panel on Antiresorptive A (2011) Managing the care of patients receiving antiresorptive therapy for prevention and treatment of osteoporosis: executive summary of recommendations from the American Dental Association Council on Scientific Affairs. J Am Dent Assoc 142:1243–1251
11. Pasion EG, Sivananthan SK, Kung AW, Chen SH, Chen YJ, Mirasol R, Tay BK, Shah GA, Khan MA, Tam F, Hall BJ, Thiebaud D (2007) Comparison of raloxifene and bisphosphonates based on adherence and treatment satisfaction in postmenopausal Asian women. J Bone Miner Metab 25:105–113. https://doi.org/10.1007/s00774-006-0735-7
12. Gennari L, Rotatori S, Bianciardi S, Nuti R, Merlotti D (2016) Treatment needs and current options for postmenopausal osteoporosis. Expert Opin Pharmacother 17:1141–1152. https://doi.org/10.1080/14656566.2016.1176147
13. Valderas JM, Kotzeva A, Espallargues M, Guyatt G, Ferrans CE, Halyard MY, Revicki DA, Symonds T, Parada A, Alonso J (2008) The impact of measuring patient-reported outcomes in clinical practice: a systematic review of the literature. Qual Life Res 17:179–193. https://doi.org/10.1007/s11136-007-9295-0
14. Alan Brookhart JA, Katz JN, Finkelstein JS, Arnold M, Polinski JM, Patrick AR, Mogun H, Solmon DH (2007) Gaps in treatment among users of osteoporosis medications: the dynamics of noncompliance. Am J Med 120:251–256

15. Sweileh WM, Ihbesheh MS, Jarar IS, Taha AS, Sawalha AF, Zyoud SH, Jamous RM, Morisky DE (2011) Self-reported medication adherence and treatment satisfaction in patients with epilepsy. Epilepsy Behav 21:301–305. https://doi.org/10.1016/j.yebeh.2011.04.011
16. Zyoud SH, Al-Jabi SW, Sweileh WM, Morisky DE (2013) Relationship of treatment satisfaction to medication adherence: findings from a cross-sectional survey among hypertensive patients in Palestine. Health Qual Life Outcomes 11:191. https://doi.org/10.1186/1477-7525-11-191
17. Miyakoshi N, Kudo D, Hongo M, Kasukawa Y, Ishikawa Y, Shimada Y (2017) Comparison of spinal alignment, muscular strength, and quality of life between women with postmenopausal osteoporosis and healthy volunteers. Osteoporos Int. https://doi.org/10.1007/s00198-017-4184-z
18. Madureira MM, Ciconelli RM, Pereira RM (2012) Quality of life measurements in patients with osteoporosis and fractures. Clinics (Sao Paulo) 67:1315–1320
19. Baczyk G, Samborski W, Jaracz K (2016) Evaluation of the quality of life of postmenopausal osteoporotic and osteopenic women with or without fractures. Arch Med Sci 12:819–827. https://doi.org/10.5114/aoms.2015.55012
20. Ringe JD, Moller G (2009) Differences in persistence, safety and efficacy of generic and original branded once weekly bisphosphonates in patients with postmenopausal osteoporosis: 1-year results of a retrospective patient chart review analysis. Rheumatol Int 30:213–221. https://doi.org/10.1007/s00296-009-0940-5
21. Carr AJ, Thompson PW, Cooper C (2006) Factors associated with adherence and persistence to bisphosphonate therapy in osteoporosis: a cross-sectional survey. Osteoporos Int 17:1638–1644. https://doi.org/10.1007/s00198-006-0166-2
22. Atkinson MJ, Sinha A, Hass SL, Colman SS, Kumar RN, Brod M, Rowland CR (2004) Validation of a general measure of treatment satisfaction, the Treatment Satisfaction Questionnaire for Medication (TSQM), using a national panel study of chronic disease. Health Qual Life Outcomes 2:12. https://doi.org/10.1186/1477-7525-2-12
23. Reynolds K, Viswanathan HN, Muntner P, Harrison TN, Cheetham TC, Hsu JW, Gold DT, Silverman S, Grauer A, Morisky DE, O'Malley CD (2014) Validation of the Osteoporosis-Specific Morisky Medication Adherence Scale in long-term users of bisphosphonates. Qual Life Res 23:2109–2120. https://doi.org/10.1007/s11136-014-0662-3
24. Lee YK, Nam HS, Chuang LH, Kim KY, Yang HK, Kwon IS, Kind P, Kweon SS, Kim YT (2009) South Korean time trade-off values for EQ-5D health states: modeling with observed values for 101 health states. Value Health 12:1187–1193. https://doi.org/10.1111/j.1524-4733.2009.00579.x
25. Voko Z, Gaspar K, Inotai A, Horvath C, Bors K, Speer G, Kalo Z (2017) Osteoporotic fractures may impair life as much as the complications of diabetes. J Eval Clin Pract 23:1375–1380. https://doi.org/10.1111/jep.12800
26. Kuo SZ, Haftek M, Lai JC (2017) Factors associated with medication non-adherence in patients with end-stage liver disease. Dig Dis Sci 62:543–549. https://doi.org/10.1007/s10620-016-4391-z
27. Espallargues M, Valderas JM, Alonso J (2000) Provision of feedback on perceived health status to health care professionals: a systematic review of its impact. Med Care 38:175–186
28. Turbi C, Herrero-Beaumont G, Acebes JC, Torrijos A, Grana J, Miguelez R, Sacristan J, Marin F (2004) Compliance and satisfaction with raloxifene versus alendronate for the treatment of postmenopausal osteoporosis in clinical practice: an open-label, prospective, nonrandomized, observational study. Clin Ther 26:245–256
29. Barrett-Connor E, Wade SW, Do TP, Satram-Hoang S, Stewart R, Gao G, Macarios D (2010) Treatment satisfaction and persistence among postmenopausal women on osteoporosis medications: 12-month results from POSSIBLE US™. Osteoporos Int 23:733–741
30. Mulligan R, Sobel S (2005) Osteoporosis: diagnostic testing, interpretation, and correlations with oral health—implications for dentistry. Dent Clin N Am 49:463–484. https://doi.org/10.1016/j.cden.2004.10.005
31. Warriner AH, Curtis JR (2009) Adherence to osteoporosis treatments: room for improvement. Curr Opin Rheumatol 21:356–362. https://doi.org/10.1097/BOR.0b013e32832c6aa4
32. Yood RA, Emani S, Reed JI, Lewis BE, Charpentier M, Lydick E (2003) Compliance with pharmacologic therapy for osteoporosis. Osteoporos Int 14:965–968. https://doi.org/10.1007/s00198-003-1502-4
33. Shah ND, Dunlay SM, Ting HH, Montori VM, Thomas RJ, Wagie AE, Roger VL (2009) Long-term medication adherence after myocardial infarction: experience of a community. Am J Med 122:961 e7–13. https://doi.org/10.1016/j.amjmed.2008.12.021
34. Caro JJ, Ishak KJ, Huybrechts KF, Raggio G, Naujoks C (2004) The impact of compliance with osteoporosis therapy on fracture rates in actual practice. Osteoporos Int 15:1003–1008. https://doi.org/10.1007/s00198-004-1652-z
35. Robitaille J, Yoon PW, Moore CA, Liu T, Irizarry-Delacruz M, Looker AC, Khoury MJ (2008) Prevalence, family history, and prevention of reported osteoporosis in U.S. women. Am J Prev Med 35:47–54. https://doi.org/10.1016/j.amepre.2008.03.027
36. Hong SM, Choi WH (2011) Osteoporosis and decrease in bone mineral density have associated with the reduced quality of life. Osteoporosis 9:175–179
37. Dhillon V, Hurst N, Hannan J, Nuki G (2005) Association of low general health status, measured prospectively by Euroqol EQ5D, with osteoporosis, independent of a history of prior fracture. Osteoporos Int 16:483–489. https://doi.org/10.1007/s00198-004-1705-3
38. Cranney A, Tugwell P, Adachi J, Weaver B, Zytaruk N, Papaioannou A, Robinson V, Shea B, Wells G, Guyatt G, Osteoporosis Methodology G, The Osteoporosis Research Advisory G (2002) Meta-analyses of therapies for postmenopausal osteoporosis. III. Meta-analysis of risedronate for the treatment of postmenopausal osteoporosis. Endocr Rev 23:517–523. https://doi.org/10.1210/er.2001-3002
39. Rosen CJ (2005) Clinical practice. Postmenopausal osteoporosis. N Engl J Med 353:595–603. https://doi.org/10.1056/NEJMcp043801
40. Eekman DA, Vis M, Bultink IE, Derikx HJ, Dijkmans BA, Lems WF (2009) Treatment with intravenous pamidronate is a good alternative in case of gastrointestinal side effects or contraindications for oral bisphosphonates. BMC Musculoskelet Disord 10:86. https://doi.org/10.1186/1471-2474-10-86
41. Black DM, Schwartz AV, Ensrud KE, Cauley JA, Levis S, Quandt SA, Satterfield S, Wallace RB, Bauer DC, Palermo L, Wehren LE, Lombardi A, Santora AC, Cummings SR, Group FR (2006) Effects of continuing or stopping alendronate after 5 years of treatment: the Fracture Intervention Trial Long-term Extension (FLEX): a randomized trial. JAMA 296:2927–2938. https://doi.org/10.1001/jama.296.24.2927
42. Huas D, Debiais F, Blotman F, Cortet B, Mercier F, Rousseaux C, Berger V, Gaudin AF, Cotté FE (2010) Compliance and treatment satisfaction of post menopausal women treated for osteoporosis. Compliance with osteoporosis treatment. BMC Womens Health 10:26. https://doi.org/10.1186/1472-6874-10-26

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