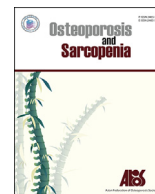




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Original article

Understanding the factors associated with initiation and adherence of osteoporosis medication in Japan: An analysis of patient perceptions

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ABSTRACT

Objectives: This study aimed to identify factors associated with initiation and adherence of osteoporosis medication from a patient perspective.**Methods:** A web-based survey was developed based on health behavior theories. Descriptive analyses were conducted for all survey items. Analyses in a structural equation modeling framework were conducted to identify factors associated with treatment initiation and adherence.**Results:** Five hundred forty-five women completed the questionnaire. A majority were currently receiving medications for osteoporosis ($n = 376$, 69.0%) and 25.0% of these patients ($n = 94$) were considered adherent to their treatment. Knowledge was strongly associated with osteoporosis treatment initiation (standard error [SE], 0.58). Greater knowledge of disease was associated with increased likelihood of initiating medication. Medication complexity (SE, 0.49) and perceived susceptibility to fracture and loss of independence (SE, -0.37) were also associated with initiation. Perceived barriers (SE, -0.85) such as inconvenience, lack of efficacy and financial burden were observed to be the greatest obstacle to adherence. The greater the perceived barriers, the less likely patients were to adhere to medication. Patients' perception of self-efficacy (SE, 0.37) also affected adherence. The greater the patient perception of ability to independently manage their medication, the more likely they were to adhere to the medication.**Conclusions:** Different factors were found to be associated with initiation and adherence of osteoporosis medication. Patient knowledge of their disease and the perception of barriers were found to be the most influential. Empowering patients with the knowledge to better understand their disease and decreasing the perception of barriers through education initiatives may be effective in improving patient outcomes.© 2017 The Korean Society of Osteoporosis. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Osteoporosis is clinically characterized by an increased risk of fracture due to compromised bone strength and a reduction in bone mass [1,2]. In Japan, the prevalence of osteoporotic patients aged 40 or above was estimated to have reached 12.8 million in 2012, and 9.8 million among them were women [3]. The estimated annual incidence of osteoporosis in Japan was reported to be 0.6% in men

and 2.3% in women, resulting in approximately 970,000 incident cases (160,000 men and 810,000 women) per year [3].

Osteoporosis leads to decreased quality of life (QoL) for patients, due to comorbidities, level of independence and morbidity, and complications [4,5]. QoL is significantly decreased when a patient experiences a fracture, and decreases in QoL following vertebral fractures, lumbar fractures, and hip fractures have been repeatedly documented in the literature [4]. While evidence from Japan has shown that approximately 148,100 individuals (31,300 men and 116,800 women) sustained proximal femoral fractures due to osteoporosis in 2007, recent estimates of the incidence of hip fractures in 2012 totaled 175,700 (37,600 men and 138,100 women), a 19% increase compared to 2007 [5]. In addition to reductions in QoL, osteoporosis is also associated with a substantial

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economic burden. In the United States, the cost of osteoporosis-related fractures was estimated to be approximately US \$17 billion in 2005 and was projected to grow by approximately 48%, incurring more than US \$25.3 billion by 2025 [6]. In Europe, the economic burden of incident and prior fragility fractures was estimated to reach €37 billion [7]. Although osteoporosis-related economic data in Japan are scarce, recent estimates have reported that the per-patient burden of hip fracture was US \$25,599 in treatment costs per fracture event and in excess of US \$43,755 per year for nursing care [8]. A similar pattern of high cost has been reported in other countries in Asia [9,10].

The 2011 Japanese osteoporosis guidelines state that the goals of osteoporosis treatment are prevention of fracture and maintenance of good skeletal health [3]. A recent review of osteoporosis studies has consolidated evidence that drug therapy can reduce osteoporosis-related fracture risk in patients over 50 years of age [11]; however, medication effectiveness has been limited due to low treatment rate and poor medication adherence [11]. Evidence from multiple countries, together with evidence from Japan [12] has shown that poor adherence to osteoporosis medication is associated with a high risk of fracture, high medical costs and/or a high frequency of hospitalization [11]. In contrast, good adherence can help achieve better therapeutic benefit [13]. The association between fracture rate reduction and good adherence has been reported in numerous previous studies [11,14–16].

Real world adherence to osteoporosis therapy has been reported to be low both globally and in Japan [11,17]. The results of a recent review of osteoporosis studies reporting treatment persistence and adherence with bisphosphonates suggested that less than 50% of patients remained on therapy after 1 year [11]. The primary explanation for this poor treatment persistence and adherence was the presence of mild adverse effects, dosing frequency, and costs. In Japan, it has been estimated that only 20% of osteoporosis patients actively seek treatment [18]. Furthermore, osteoporosis treatment persistence and adherence have been reported to vary with approximately 28%–60% of patients discontinuing their daily medication after 1 year [16,19–21] and 39%–61% of patients considered to be adherent to their daily treatment at 1 year [16,19].

To understand why some patients do not initiate treatment and why some patients do not adhere to their prescribed medication, it is important to obtain insights on patients' perspectives, decision making processes, particularly in regard to the complexity of variables influencing treatment initiation and adherence outcomes. The past decade has seen a growth in the use of sophisticated analytical techniques such as structural equation modeling (SEM) to address these questions in the research of social and behavioral sciences. SEM techniques use a combination of statistical data and qualitative causal assumptions to test causal relations [22]. An increasing number of studies have utilized SEM in the medical sciences to learn about patient behaviors and decision making related to pharmacological and psychotherapeutic treatments in various therapeutic areas including oncology, infectious diseases, diabetes, cardiovascular diseases, and osteoporosis [23–25].

Medication initiation and adherence are complex, multifactorial and individual behaviors. Patient perception of medication effectiveness, safety, and necessity have been previously reported to be obstacles of medication adherence in osteoporosis [26]. In a study evaluating the influence of patient characteristics, perceptions, knowledge and beliefs about osteoporosis on the decision to initiate osteoporosis treatment, knowledge of osteoporosis and beliefs in the benefits of medications were reported to have a positive impact on medication initiation [27]. Patients who had started treatment were also more likely to believe in the effectiveness of osteoporosis medication and less likely to worry about side-effects of the medication [27]. Improved patient education,

availability of better tolerated and less frequently-dosed medications, and increased health care provider-patient interaction could possibly improve patient adherence [26]. This narrative-based approach to facilitating treatment adherence focusing on the perspective of each individual patient can help to improve patient-centered treatment and management of osteoporosis. Such an approach would be helpful in supporting existing evidence-based medicine to reach its full potential.

The aim of this study was to identify the factors that are associated with treatment initiation and adherence of osteoporosis medication using a patient internet survey based on health behavior theories and analyses in a SEM framework.

2. Methods

2.1. Study participants

Study participants were recruited from a patient panel developed and managed by an internet-based research company. Eligible participants were female aged 50 years or older with a self-reported diagnosis of osteoporosis. At the screening phase of the online survey, participants were asked if they have been diagnosed with any of 16 chronic conditions presented, including osteoporosis. Only responders who reported osteoporosis were able to move forward to the full survey. Participants were excluded if they reported a diagnosis of cancer or human immunodeficiency virus due to a potentially high number of prescription drugs utilized by these patients. Participants were also excluded if they reported dementia, Alzheimer disease, or psychiatric disorders which were considered to potentially affect patients' perception and decision making processes.

2.2. Patient survey

The survey was developed specifically for this study, using a hypothesized conceptual framework based on behavioral psychology theories related to health behaviors, decision making processes, and perception of the illness and treatments [28–30]. The literature search was guided by using a combination of different keywords in PubMed or Google Scholar, including osteoporosis, health behavior model, social cognitive theory, self-regulation, and adherence. The instruments that measure these topics and have been validated in osteoporosis patients included the Osteoporosis Self-Efficacy Scale [31], the Osteoporosis Health Belief Scale [32], the Beliefs about Medicines Questionnaire, and the Osteoporosis-Specific Morisky Medication Adherence Scale 8-Item (MMAS-8) [33]. The authors believe it is important to use validated measures wherever possible, so the Osteoporosis-Specific MMAS-8 was selected to measure adherence in our study. As for other concepts, none of the instruments were validated in Japanese language or osteoporosis patients in Japan; therefore, the questions included in the original instruments were reviewed closely. The survey developed for this study contained a total of 31 questions for patients who are not currently treated with osteoporosis medications and 44 questions, including the 8 MMAS questions, for patients who are currently treated with osteoporosis medications (Supplementary Table 1).

2.3. Outcome definition and variables

There were 2 outcome measures for this study: whether patients ever initiated treatment for osteoporosis; and whether patients were adherent to osteoporosis medication. For initiation, patients who reported that they were currently or previously treated with osteoporosis medications were categorized as

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