



Drug-related problems in patients with osteoporosis

Problemi u vezi sa lekovima kod bolesnika sa osteoporozom

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Abstract

Background/Aim. Drug-related problems are especially frequent among patients suffering from non-communicable diseases, like osteoporosis, leading to suboptimal treatment response. The aim of this study was to identify drug-related problems in patients with osteoporosis. **Methods.** This cross-sectional prospective study was conducted in January 2014 on outpatients with osteoporosis from three health facilities in Belgrade, Serbia. The patients included in the study were older than 50 years, and they were offered an anonymous questionnaire with open-ended questions. **Results.** There were 355 study participants, 329 (92.7%) females and 26 (7.3%) males. The patients who experienced at least one osteoporotic fracture ($n = 208$) were significantly less adherent to the therapy, less engaged in sports and regular physical activities, and more prone to nutrition with inadequate intake of calcium and vitamin D than patients without fractures ($n = 147$). **Conclusion.** The effectiveness of osteoporosis treatment is decreased by several drug-related problems encountered by both physicians and patients. However, the majority of the drug-related problems could be greatly influenced by appropriate educational programs.

Key words: osteoporosis; risk factors; medication errors; preventive health services; questionnaires.

Apstrakt

Uvod/Cilj. Problemi zbog lekova posebno su česti kod bolesnika nezaraznim bolestima, kao što su osteoporoza, što je dovelo do suboptimalnog doziranja u lečenju. Cilj ove studije bio je da identifikuje probleme izazvane lekovima kod bolesnika sa osteoporozom. **Metode.** Ova prospektivna studija sprovedena je u januaru 2014 na bolesnicima obolelim od osteoporoze u tri zdravstvene ustanove u Beogradu, Srbija. Bolesnici uključeni u studiju bili su stariji od 50 godina i oni su popunjavali anonimne upitnike sa otvorenim pitanjima. **Rezultati.** Od 355 učesnika, 329 (92,7%) bile su osobe ženskog pola, a 26 (7,3%) muškog. Bolesnici koji su imali makar jedan prelom zbog osteoporoze ($n = 208$) statistički značajno manje su pristalice terapije, manje su se bavili sportom i redovnim fizičkim aktivnostima, a više su bili skloni ishrani sa neadekvatnim unosom kalcijuma i vitamina D, nego bolesnici bez preloma ($n = 147$). **Zaključak.** Efikasnost lečenja osteoporoze snižena je zbog nekoliko problema u vezi sa lekovima sa kojima se susreću kako lekari, tako i bolesnici. Međutim, na većinu problema u vezi sa lekovima moglo bi se u velikoj meri uticati odgovarajućim obrazovnim programima.

Ključne reči: osteoporoza; faktori rizika; lečenje, greške; preventivno-medicinska zaštita; upitnici.

Introduction

Drug-related problems include adverse drug reactions and errors in prescribing, dispensing or administering drugs, regardless of who made the error, health worker or patient¹. Such problems are especially frequent among patients suffering from non-communicable diseases². Among the non-communicable diseases that affect European population, osteoporosis is one of the most prevalent, creating heavy economical burden for all societies. About 6% of men and 21% of women aged 50–84 years have osteoporosis in European

Union; osteoporotic fractures, which are the main clinical consequence of osteoporosis, will be experienced during the remaining lifetime by 22% of men and 46% of women who are older than 50 years³. Serbian health system is facing similar burden, since only one of the osteoporotic fractures, hip fracture, has annual incidence rate of 143.6 *per* 100,000 inhabitants older than 50 years⁴.

Drug-related problems in patients with osteoporosis are frequent, but under-investigated⁵. Under-prescribing of vitamin D supplementation was noted in 54.2% of patients at high risk of osteoporosis⁶, and even 32.3% of patients taking

oral bisphosphonates experience adverse effects⁷. A special problem is the persistence with bisphosphonates therapy, which was as low as 80% after 2 years in a group of patients from Malaysia⁷. The persistence with prescribed therapy is higher among patients with more severe forms of osteoporosis, and improves with the duration of treatment course^{8,9}. Among the elderly patients with osteoporosis, almost 16% is not being prescribed drug therapy, and this type of drug-related problem is more frequent in patients who live in their homes than in residents of nursing homes¹⁰. Yet, we know very little about factors that are associated with drug-related problems in patients with osteoporosis, and therefore our ability to undertake some preventive measures is limited.

The aim of this study was to identify drug-related problems in patients with osteoporosis and reveal characteristics of the patients and/or prescribed treatments which are associated with the drug-related problems.

Methods

This cross-sectional prospective study was conducted in January 2014 on outpatients with osteoporosis from three health facilities in Belgrade, Serbia: Osteoporosis Center of Orthopedic Institute "Banjica", Osteoporosis Department of Clinical Ward for Endocrinology, Diabetes and Metabolic Diseases, Clinical Hospital Center "Zvezdara" and Osteoporosis Counseling Unit of Primary Health Center "Savski Venac". Patients older than 60 years with diagnosis of osteoporosis who visited these three facilities during the study period were included in the study; only patients with cognitive disturbances or psychiatric diseases were excluded. The patients were offered an anonymous questionnaire with open-ended questions, specially designed for this study, after they completed their encounter with a rheumatologist.

The anonymous questionnaire had the following questions: about socio-demographic characteristics (age, sex, weight, occupation, place of residence, etc.); about clinical course of osteoporosis (duration of illness, treatment duration, number of previous fractures, etc.); about medication for osteoporosis (names of drugs that the patients used for treatment of osteoporosis, daily doses of these drugs, duration of use of these drugs, whether the patient had adverse effects); about treatment and therapy of chronic diseases unrelated to osteoporosis (the existence of other chronic diseases unrelated to osteoporosis and their treatment regimens, previous hospitalizations, etc.); about patients' nutrition (intake of foods rich in calcium and vitamin D, alcohol consumption, consuming more than 4 cups of coffee *per* day, frequent intake of carbonated soft drinks, etc.).

The approval for this study was obtained from the Ethics Committee of Faculty of Medical Sciences, University of Kragujevac.

The data collected by the questionnaire were at first described using measures of central tendency (mean and median) and variability (standard deviation) for continuous variables, and percentages for categorical variables. The significance of differences in continuous variables between the patients who experienced an osteoporotic fracture and those

who did not was tested by Student's *t*-test for large independent samples. The differences in categorical variables were tested by χ^2 test. The differences were considered significant if the probability of null hypothesis was lower than 0.05. All calculations were performed by statistical software SPSS, version 18.

Results

The study included 355 patients, 329 (92.7%) females and 26 (7.3%) males; 70 (19.7%) of them were between 60 and 65 years, 245 (69.0%) were between 70 and 75 years, and 40 (11.3%) patients were 75 to 80 years old. There were 208 (58.6%) patients who experienced osteoporotic fractures [196 (94.2%) females and 12 (5.8%) males] and 147 (41.4%) patients with no fractures [133 (90.5%) females and 14 (9.5%) males; ($\chi^2 = 1.789$; $df = 1$; $p > 0.05$); ($p = 0.181$)]. There were 120 (33.8%) patients with vertebral fractures, 85 (23.9%) patients with hip fractures, 116 (32.7%) patients with fractures of radius, 58 of them (16.3%) with fractures of humerus and 37 (10.4%) patients with pelvic fractures; 107 (30.1%) experienced one osteoporotic fracture, 56 (15.8%) two, and 45 (12.7%) had more than two fractures. Characteristics of the study participants according to experience with osteoporotic fractures are presented in Table 1.

A significant number of patients was not adherent to drug therapy for osteoporosis. The main reasons for non-adherence offered by the patients were: experience with adverse effects (48.5%), belief that anti-osteoporotic drugs create more harm than benefit (68.9%), and underestimating health consequences of osteoporosis (57.3%). The effects of adherence to signs and symptoms experienced by the patients are shown in Table 2.

Discussion

Recently, treatment options for osteoporosis have increased significantly. Although bisphosphonates are still the most utilized drugs for this disorder worldwide¹¹, new molecular entities with specific mechanism of action are now available, like teriparatide (stimulator of osteoblasts) or denosumab (inactivator of osteoclasts). Regardless of the type of anti-osteoporosis therapy, adherence to prescribed regimen remains unsolved, since only half of the patients with osteoporosis is actually taking their drug therapy as prescribed⁹. The patients in our study were also largely non-adherent, which was related to increased osteoporosis signs and symptoms.

Previously published studies showed that some of the reasons for non-adherence of patients with osteoporosis to drug therapy are experience with unpleasant gastrointestinal adverse effects of bisphosphonates¹², forgetfulness and preoccupation with other daily routines¹³. The non-adherent patients in our study also had prejudices about both osteoporosis and drug treatment. In the first place they underestimated health consequences of osteoporosis, and then they believed that drugs for osteoporosis are ineffective and unsafe. Such attitude is at least in some part the consequence of poor knowledge of patients about their disease and medications.

Table 1

Characteristics of the patients in regard to their experience with osteoporotic fractures			
Variable	The patients who experienced osteoporotic fracture (n = 208)	The patients with no osteoporotic fracture (n = 147)	<i>p</i>
Occupation, n (%)			
clarks	83 (39.9)	37 (25.2)	< 0.001
workers	55 (26.4)	73 (49.7)	
teachers	8 (3.8)	1 (0.7)	
health workers	23 (11.1)	12 (8.2)	
unemployed	39 (18.8)	24 (16.3)	
Place of living, n (%)			
city	51 (24.5)	54 (36.7)	< 0.001
suburbs	51 (24.5)	52 (35.4)	
village	106 (51.0)	41 (27.9)	
Previous engagement in sport activities, n (%)	32 (15.4)	39 (26.5)	0.010
The patients adherent to bisphosphonates, n (%)	104 (50.0)	98 (66.7)	0.002
The patients adherent to teriparatide, n (%)	32 (15.4)	146 (99.3)	< 0.001
Experienced any adverse effect of drugs for osteoporosis, n (%)	158 (76.0)	111 (75.5)	> 0.05
Regular use of food rich with vitamin D and/or calcium	20 (9.6)	122 (80.3)	0.039
Everyday use of sweet, gassed beverages	130 (62.5)	25 (17.0)	< 0.001

Table 2

Signs and symptoms of osteoporosis in regard to the patients' adherence to the prescribed drug therapy			
Sign or symptom	The patients adherent to drug therapy (n = 252)	The patients not adherent to drug therapy (n = 103)	<i>p</i>
Loss of body height, n (%)	27 (10.7)	19 (18.4)	0.049
Decreased mobility, n (%)	96 (38.1)	57 (55.3)	0.003
Pain in the extremities, n (%)	177 (70.2)	85 (82.5)	0.017

In the study by La et al.¹³ only 42.9% of patients knew exact names of drugs they were taking. The patients should be much more informed about their disease and treatment options, and all of their fears and concerns should be addressed. Not only prescribers, but also clinical and community pharmacists should be involved in this process of communication with patients suffering from osteoporosis, since it was already shown that pharmaceutical care increases medication adherence among patients with osteoporosis. In the study of Stuurman et al.¹⁴ individualized counselling sessions and continuous monitoring of medication use performed by community pharmacists led to decrease of medication non-adherence from 32.8% to 19% in patients with osteoporosis.

The consequences of treatment non-adherence in patients with osteoporosis are grave and manifest themselves as increased fracture risk. In a systematic review by Imaz et al.¹⁵ it was shown that non-adherence to prescribed therapy increases fracture risk for 46% in relation to the adherent patients.

Fractures experienced by the study patients were considered to be the consequence of osteoporosis if they happened spontaneously or were caused by minor trauma which would not cause fracture in otherwise healthy person. In patients observed in this study, the fractures were caused by bending the body, lifting light loads, by sudden movements, and sometimes without any obvious reason.

The patients with osteoporotic fractures from our study were much more non-adherent to bisphosphonates or teriparatide than the patients without fractures. The number and percentage of patients with or without fractures, depended among other things on the profession and place of residence of the respondents. The distribution of the respondents without fractures according to their profession was as the following: workers, clarks, unemployed, health workers and teachers. Such result was expected, since physical activity delays progression of osteoporosis. Our analysis also show that the majority of patients who did not have fractures caused by osteoporosis came from urban areas, while the minority came from rural areas. The reason for this difference could be found in lower access of rural population to healthcare service, and therefore lower treatment rate and lower treatment adherence.

The increase in fracture rate is associated with great increases in mortality and healthcare costs, since treatment of fractures requires hospitalization and surgical interventions¹⁶. In our study, the largest percentage of respondents had vertebral fractures, which are difficult to treat and bear high treatment costs.

General signs and symptoms of osteoporosis are also more pronounced in non-adherent patients: in our study loss of body height and decreased mobility were more frequent in

the patients who did not take their therapy as prescribed. Increased occurrence of osteoporosis symptoms is associated with lower quality of life, as already shown in the literature¹⁷.

Regular and moderate physical activity has protective effect against osteoporosis and occurrence of fractures. This is the consequence of both direct beneficial effect on bone metabolism and on improved balance, coordination and muscle strength, contributing to prevention of falls^{18,19}. Fractures were less frequent in the groups of our patients that were engaged in sport activities and employed as physical workers, probably because prolonged physical activity in the past improved their coordination and muscle strength, making them less prone to falls. However, since beneficial effects of physical activity on osteoporosis are not age-limited, even elderly patients with overt osteoporosis should be enrolled in tailored physical activity programs. It was recently shown that fracture-preventing programs in patients with osteoporosis which include physical activity are the most cost/effective²⁰.

Besides regular physical activity and osteoporosis medication, appropriate nutrition providing for sufficient intake of vitamin D and calcium is also important for prevention of osteoporosis and its complications. It was shown previously that bone mineral density in postmenopausal women is positively correlated with intake of dairy products rich in calcium and vitamin D²¹. This was noted also in our study,

since patients with fractures far less regularly ate food rich in calcium and vitamin D, and far more frequently used sweet and gassed beverages whose nutritional value is very low. A lot of studies demonstrated effectiveness of educational interventions on improvement of nutrition in patients with osteoporosis²², and education of patients about adequate nutrition should be implemented in everyday clinical practice.

Conclusion

The effectiveness of osteoporosis treatment is decreased by several drug-related problems encountered by both physicians and patients: adverse drug reactions, non-adherence to the treatment, prejudices of patients towards drug efficacy and safety, and non-adherence to appropriate diet and regular physical activity. Much should be done on education of patients with osteoporosis, since the majority of the drug-related problems could be greatly influenced by appropriate educational programs.

Acknowledgements

This study was partially supported by the grant No 175007 from the Serbian Ministry of Education, Science and Technological Development and by grant No 404 from the Montenegrin Ministry of Science.

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Received on September 09, 2014.

Revised on February 18, 2015.

Accepted on February 24, 2015.

Online First September, 2015.