ORIGINAL RESEARCH

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How to Treat Osteoporosis in Octogenarians?

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Abstract

Objective: There are few studies investigating the efficacy of anti-osteoporotic drugs in the oldest old. This study aimed to compare the effectiveness of osteoporosis treatment among individuals older and younger than 80 years of age.

Materials and Methods: A total of 257 patients with osteoporosis, aged 65 and over, 234 women and 23 men, were included in the study. Sixty-five of the patients were aged 80 years and older. Seventy-four participants received alendronate, 93 received zoledronic acid, and 90 received denosumab. Dual-energy X-ray absorptiometry scans were performed at baseline and at month 24.

Results: The proportion of the participants receiving glucocorticoid was higher in the under 80-age group. Bone mineral density (BMD) changes were similar between the <80 and ≥80 aged groups. There was no significant difference in the lumbar spine and femoral neck BMD changes between the groups in terms of the anti-osteoporotic agent used. A statistically significant strong positive correlation was found between the femur neck BMD change and fracture risk reduction percentage.

Conclusion: This study showed that osteoporosis treatment in individuals over 80 years of age is as effective as in those under 80 years of age. The results of our study may guide osteoporosis treatment in older individuals.

Keywords: Osteoporosis, oldest old, bisphosphonates, denosumab

Introduction

Osteoporosis is a common chronic disease with a significant global burden characterized by low bone mass, skeletal fragility, and microarchitectural deterioration (1). It is defined as a fragility fracture and/or a T-score of -2.5 or lower and is an important cause of morbidity and mortality among older adults (2).

Pharmacologic agents for the treatment of osteoporosis can be classified as either antiresorptive (alendronate, zoledronate, and denosumab) or anabolic (teriparatide and abaloparatide). Alendronate is an antiresorptive agent commonly used as first-line therapy for osteoporosis and effectively reduces the risk of vertebral, non-vertebral, and hip fractures (3). Zoledronate is administered by intravenous injection at intervals of one year and has anti-fracture efficacy and positive effects on bone mineral density (BMD) in older adults with osteoporosis (4). Denosumab inhibits bone resorption by binding to the receptor activator of the nuclear factor-κβ ligand, thereby decreasing the differentiation of osteoclasts. Denosumab reduces the risk of hip, non-vertebral, and vertebral fractures (5).

In many countries, the number of patients with osteoporosis is expected to increase with societal aging. In addition, as the number of individuals over 80 years increases, the risk of osteoporotic fractures increases correspondingly (6). Little is known about the efficacy of osteoporosis medication in octogenarians.

Several studies have highlighted a significant association between increasing age and a reduced likelihood of receiving effective osteoporosis treatment (7-9). A large meta-analysis study including patients with a median age of 64 years has showed that denosumab, zoledronic acid, and alendronate had similar fracture risk reduction with small differences in efficacy (10).

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In this study, we aimed to investigate the effect of osteoporosis treatment agents on the BMD change and fracture risk reduction among patients with osteoporosis older and younger than 80 years of age.

Materials and Methods

Participants

A total of 274 patients aged 65 and over who applied to our outpatient clinic and were diagnosed with osteoporosis were included in this retrospective study. Exclusion criteria were renal impairment, primary or metastatic bone tumor, and bone diseases other than osteoporosis. BMD measurement of the lumbar spine and proximal femur was performed by DXA method (using Hologic scanners) before the treatment and at month 24. Seventeen patients without a DXA scan at month 24 were excluded. The percent change from the baseline BMD was calculated at month 24. Alendronate was administered 70 mg/weekly oral, zoledronic acid 5 mg/yearly intravenous, and denosumab 60 mg/every 6 months subcutaneously. All patients were prescribed 1000 mg of calcium and 800 IU of vitamin D per day. Glucocorticoid (GC) use was considered as use of ≥5 mg/day prednisolone or equivalent for 3 months or more. Approval for the study was granted by the Gaziantep University Local Ethics Committee (no: 2020/422 dated 24.02.2021).

Statistics

Statistical analyses were performed with SPSS for Windows version 22.0 (IBM SPSS Statistics, Armonk, NY). The distribution of normality was checked using the Shapiro-Wilk test. We used the independent samples t-test and Mann-Whitney U test to compare two independent groups of variables, the chi-squared test to assess the relationship between categorical variables, and Spearman's rank correlation coefficients between numerical variables. A p-value less than 0.05 was accepted as statistically significant.

Results

The median age of the 257 patients was 69 years, 65 of them were over 80 years old, and 91.1% were women. Eighteen were smokers and none of them had alcohol consumption. The proportion of those receiving GC was higher in the under 80 age group. There was no significant difference between the groups in terms of laboratory analysis results. The proportion of those receiving zoledronic acid and denosumab was higher in the ≥80 age group, although there was no statistically significant difference (Table 1).

Baseline BMD and T-scores of the femoral neck were lower in the ≥80 age group, while BMD changes did not differ between the age groups (Table 2). There was no statistically significant difference in BMD changes between the groups in terms of the anti-osteoporotic agent used (Table 3).

Age, number of comorbidities, and medications were not correlated with the BMD change and fracture risk reduction. A statistically significant strong positive correlation was found between femur neck BMD change and percentage reductions in major osteoporotic and hip fracture risk. In addition, there was a statistically significant negative correlation between the baseline femur neck BMD and the BMD changes and fracture risk reduction, also between the baseline lumbar spine BMD and lumbar spine BMD changes (Table 4).

Discussion

We aimed to investigate the effectiveness of osteoporosis treatment in individuals over 80 years, who often are not included in clinical trials. Our findings have shown that response to the osteoporosis treatment agents according to the BMD and fracture risk reduction did not differ in individuals younger or older than 80 years.

Senile osteoporosis is characterized by loss of cortical bone and trabecular bone, and hence a decrease in BMD in regions rich in cortical bone such as the proximal femur, pelvis, and humerus. This may explain why the participants over the age of 80 had lower BMDs of the femoral neck than those under the age of 80 in our study (11).

With an increasingly aging population, there is a strong interest in the efficacy of treatment agents in older osteoporotic adults (12,13). However, there is little clinical evidence of the effectiveness of osteoporosis treatment in different age groups. In this study, it was shown that the efficacy of alendronate, zoledronic acid, and denosumab continued in advanced ages.

Multimorbidity and polypharmacy, which are common conditions in older individuals, may complicate compliance with oral antiosteoporotic drugs. In addition, parenteral agents may be preferred more frequently in elderly osteoporosis, since gastrointestinal absorption of oral agents may decrease with age, and zoledronic acid and denosumab have longer dose intervals and can largely eliminate compliance and persistence problems. The relatively higher preference for parenteral treatments in our study may be due to these factors.

A previous study has shown that that alendronate effectively reduces the risk of fractures in vertebral fractures in women aged 55-81 years with low BMD (14). Another study reported that alendronate was effective in reducing the risk of osteoporotic fractures, regardless of age (15).

Zoledronic acid treatment, administered intravenously 5 mg once a year for 3 years, was also effective in patients 75 years of age and older with osteoporosis and significantly reduced the risk of vertebral and nonvertebral fractures (16).

Table 1. Socio-demographic characteristics and laboratory analysis results of the participants

	Aged <80 years (n=192)	Aged ≥80 years (n=65)	p	Total (n=257)
Gender				
Female	176 (91.7%)	58 (89.2%)	0.616	234 (91.1%)
Male	16 (10.8%)	7 (10.8%)		23 (8.9%)
Age (years)#	67	82	<0.001*	69
Treatment agent				
Alendronate	62 (32.3%)	12 (18.5%)	0.084	74 (28.8%)
Zoledronic acid	68 (35.4%)	25 (38.5%)		93 (36.2%)
Denosumab	62 (32.3%)	28 (43.1%)		90 (35.0%)
Other comorbidities				
Hypertension	76 (39.6%)	29 (44.6%)	0.476	105 (40.9%)
Diabetes mellitus	40 (20.8%)	18 (27.7%)	0.253	58 (22.6%)
Coronary artery disease	24 (12.6%)	8 (12.3%)	0.957	32 (12.5%)
Glucocorticoid-user	40 (20.8%)	6 (9.2%)	0.039*	46 (17.9%)
Cancer	11 (5.7%)	4 (6.2%)	0.900	15 (5.8%)
Smoker	15 (7.8%)	3 (4.6%)	0.383	18 (7.0%)
Serum 25-OH vitamin D (nmol/L)†	35.6±6.1	34.0±5.5	0.169	35.2±6.2
Parathyroide hormone (pg/mL) #	58	69	0.941	60
Serum calcium (mg/dL)† ‡	9.7±0.6	9.6±0.5	0.640	9.7±0.5
Serum phosphorus (mg/dL)†	3.7±0.6	3.6±0.4	0.601	3.7±0.5
C-reactive protein (mg/dL)#	2.9	3.0	0.828	3.0
Erythrocyte sedimentation rate (mm/hr)#	17	20	0.546	18
Serum creatinine (mg/dL)#	0.65	0.68	0.221	0.66

*p≤0.05, #Data are presented as median, †Data are presented as mean ± standard deviation, ‡Albumin-adjusted calcium

Table 2. Comparison of the DXA scan assessments, BMD changes and fracture risk reduction

	Aged <80 years (n=192)	Aged ≥80 years (n=65)	p	Total (n=257)
Lumbar spine				
Baseline T-score#	-2.83±0.59	-2.74±0.78	0.394	-2.80±0.67
Baseline BMD (g/cm^2) #	0.74±0.06	0,75±0.12	0.403	0.74±0.08
24th month BMD (g/cm^2) #	0.77±0.07	0,77±0.12	0.765	0.77±0.08
BMD change (%)†	4.35 (-1.27-16.93)	3.00 (-1.35-17.64)	0.116	3.99 (-1.35-17.64)
Baseline T-score#	-2.28±0.64	-2.70±0.81	0.000*	-2.39±0.71
Baseline BMD (g/cm^2) #	0.59±0.07	0,55±0.09	0.000*	0.58±0.08
24th month BMD (g/cm^2)#	0.61±0.07	0,57±0.09	0.000*	0.60±0.08
BMD change (%)†	2.69 (-1.89-23.25)	3.69 (-1.50-28.93)	0.215	2.81 (-1.89-28.93)
Major osteoporotic fracture risk reduction (%)†	6.67 (-11.24-47.86)	9.09 (-9.09-50.00)	0.734	7.85 (-11.24-50.00)
Hip fracture risk reduction (%)†	12.25 (-3.85-68.66)	10.31 (-4.23-57.28)	0.950	11.76 (-4.23-68.66)

*p≤0.05, BMD: Bone mineral density, #Data are presented as mean ± standard deviation, †Data are presented as median (min-max)

Denosumab has been shown to significantly reduce the risk of hip fracture in elderly patients aged 75 years and older at high risk of fracture (17). In a study involving 3.902 participants receiving denosumab treatment, it was shown that age was not an important factor in terms of treatment effectiveness in individuals under 75 years of age and older (18). Anabolic agents, particularly teriparatide, have also been shown to have similar efficacy in older adults (19,20).

According to the results of our study, it was thought that the similar BMD response in both age groups might be due to the higher number of GC-users. However, there was no

Table 3. Comparison of the BMD changes between treatment agents

Treatment agent		Lumbar spine BMD change (%)	p	Femur neck BMD change (%)	p
Alendronat (n=74)	Aged <80 years (n=62)	3.63	0.189	1.85	0.509
	Aged ≥80 years (n=12)	1.34		3.27	
Zoledronic acid (n=93)	Aged <80 years (n=68)	4.33	0.469	2.83	0.815
	Aged ≥80 years (n=25)	4.44		3.03	
Denosumab (n=90)	Aged <80 years (n=62)	4.77	0.261	3.00	0.153
	Aged ≥80 years (n=28)	2.83		5.96	

BMD: Bone mineral density, data are presented as median

Table 4. Correlation analysis results between femur neck and lumbar spine BMD changes and major osteoporotic and hip fracture risk reduction

		Baseline femur neck BMD	Baseline lumbar spine BMD	Femur neck BMD change (%)	Lumbar spine BMD change (%)	Major osteoporotic fracture risk reduction (%)	Hip fracture risk reduction (%)
Baseline femur neck BMD	r p	1.000	0.226 0.000*	-0.292 0.000*	-0.004 0.943	-0.335 0.000*	-0.274 0.000*
Baseline lumbar spine BMD	r p	0.226 0.000*	1.000	-0.043 0.414	-0.232 0.000*	-0.054 0.302	-0.019 0.718
Femur neck BMD change (%)	r p	-0.292 0.000*	-0.043 0.414	1.000	0.109 0.037*	0.962 0.000*	0.961 0.000*
Lumbar spine BMD change (%)	r p	-0.004 0.943	-0.232 0.000*	0.109 0.037*	1.000	0.103 0.050*	0.101 0.053
Major osteoporotic fracture risk reduction (%)	r p	-0.335 0.000*	-0.054 0.302	0.962 0.000*	0.103 0.050*	1.000	0.953 0.000*
Hip fracture risk reduction (%)	r p	-0.274 0.000*	-0.019 0.718	0.961 0.000*	0.101 0.053	0.953 0.000*	1.000

r: Spearman rank correlation coefficient, *Significant at 0.01 level, BMD: Bone mineral density

significant difference in BMD change between GC-users and non-users, and age groups, according to treatment agents.

Study Limitations

Our study has some limitations. First, there was a lack of bone turnover markers measurement in our study. Second, a longer follow-up with a higher number of patients could better demonstrate the differences in fracture incidence. Despite these limitations our study has some strengths. First, it focuses on individuals 80 years of age and older, who are often excluded from clinical trials, but are at the highest risk of fracture. Second, we compared the effects of treatment agents among themselves, while most previous studies compared the effects of the drugs with placebo. Third, the similarity of comorbidities, inflammatory markers, and other laboratory measurements between the groups was important to compare the treatment agents more transparently.

Conclusion

The current study showed that different osteoporosis treatment agents are effective in reducing BMD and fracture risk in elderly individuals with osteoporosis aged 80 years and over. Age has not been found to affect the effectiveness of osteoporosis treatment in elderly individuals with osteoporosis. This study provides information that can guide future studies of the treatment of osteoporotic adults 80 years of age and older.

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Ethics

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Local Ethics Committee (Gaziantep University, no: 2020/522, date: 24.02.2021).

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Authorship Contributions

Concept: A.Ç., E.M.E., Design: Z.A.Ö., Data Collection or Processing: A.Ç., E.Ö., Analysis or Interpretation: A.Ç., Z.A.Ö., Literature Search: E.Ö., E.M.E., Writing: A.Ç., E.Ö.

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