The effect of vitamin d deficiency on osteoarthritis and bone mineral densities in elderly female and male patients

Vitamin d deficiency in osteoarthritis and bone mineral density changes

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Abstract

Aim: In this study, we aimed to determine the effect of inadequate vitamin D level on osteoarthritis (OA) and bone mineral density (BMD) in female and male elderly patients with early and late stage OA with different BMD, and also the relationship between vitamin D and knee function scores in female and male OA patients. Material and Method: One hundred and forty two- female and one hundred thirty-five male knee OA patients were enrolled in the study. The knee OA was classified as an early and late stage. WOMAC index, KOOS score, BMD and Vitamin D levels were measured. Multiple Logistic Regression Analyses were applied for the relationship of knee function score in female and male OA patients. Results: Vitamin D levels patients were statistically significantly lower in female OA than male OA group. Calcium and phosphorus levels were significantly higher in female OA patients than male OA group. There was no difference between vitamin D, vitamin B12, calcium, phosphorus, WOMAC index and KOOS scores in early and late stage OA patients with osteoporosis, osteopenia, and normal BMD. WOMAC index was significantly higher in male patients with osteoporosis early stage and late stage OA than patients with osteopenia and normal BMD. The age odds ratio (OR) was 1,047 (95% CI = 1,009-1,086) in female OA patients, and OR was 1.090 (95% CI = 1,021-1,163) in male OA patients. Discussion: Vitamin D supplementation may be said to increase BMD, slow down the progression of osteoporosis, reduce pain, but have no effect on OA progression and knee function scores.

Keywords

Vitamine D Deficiency; Osteoartritis; Bone Mineral Density; WOMAC Index; KOOS Score

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Introduction

Knee Osteoarthritis (OA) is the most common disabling diseases among elderly people. Prevalence of knee OA is higher in females (13%) compared to males (10%) aged ≥60 [1]. Another important problem of the elderly population, especially postmenopausal women, is the decrease in bone mineral density (BMD).Vitamin D plays a role in regulation of calcium metabolism, osteoblastic activity, matrix ossification and articular cartilage turnover [2]. It is well known that osteoarthritis and osteoporosis are positively associated with aging and that both diseases are due to bone metabolism.Although vitamin D deficiency is associated with osteoporosis and fractures in elderly women and men, the role of vitamin D deficiency is unclear in the pathogenesis of OA [3]. Vitamin D gene polymorphisms related to studies showed that osteoporosis and OA may be related diseases [4]. Insufficient D vitamin levels have been demonstrated in patients with osteoporosis [5]. Bergink et al. reported that the intake of low vitamin D supplementation could improve the progression of OA and particularly the improvement of the vitamin D status in the elderly could protect against the development and worsening of knee OA in those with low BMD [6]. McAlindon et al. reported that symptomatic knee OA patients were given vitamin D supplementation and were followed for 2 years, and also they showed that OA patients who were receiving vitamin D supplementation had no reduction in knee function [7].

The role of vitamin D on bone metabolism should be discussed in terms of the role of OA and BMD. In our study, we aimed to determine the effect of inadequate vitamin D level on OA and BMD in female and male elderly patients with early- and late-stage OA with different BMD, and also to determine the relationship between vitamin D and knee function scores in female and male OA patients.

Material and Method

One hundred and two female and one hundred thirty-five male knee OA patients were recruited consecutively from the outpatient clinic of Orthopedics between 2016 and 2018. The diagnosis of knee OA determined by radiographic features, the Kellgren, and Lawrence (K&L) scale was chosen by the World Health Organization as the accepted reference Standard [8]. Knee OA patients were classified early (stage0, stage1 and stage2) and late stage (stage 3 and stage 4) OA. The patients were homogenized for body mass index (BMI). A dual-energy X-ray absorptiometry method (DXA, Stratos dR 2D Fan Beam Dexa, DMS GROUP) was used to evaluate BMD measurements of male and female OA patients over the past year and a T-score was determined. Specifically, bone density (BMD; g/cm2) was measured at the posterior-anterior lumbar spine (L1-L4) and hip (femoral neck, trochanter, and intertrochanter space). Osteoporosis and osteopenia were defined as location-specific T-scores ≤ -2.5 and between −2.5 and −1, respectively [9].

Exclusion criteria included using systemic steroids and intraarticular hyaluronic acid injections treatment, using D vitamin supplement, infectious diseases, total knee arthroplasty or other forms of knee surgery, septic arthritis, rheumatoid arthritis, obesity, neurological or neuromuscular diseases, bone tumor, chemo- or radiotherapy for any reason, diabetes or Addison's disease and patients using any bisphosphonate or selective estrogen receptor modulator over the past year. Patients whose D vitamin levels were above the values in the max reference range were not included in the study because they did not have vitamin D insufficiency. All participants provided the written informed consent and the study protocol was approved by the local ethics committee of our hospital (10120008/05.12.2017). Clinical examination was performed and anthropometric measurements were recorded for all participants included in the study. BMI was calculated in kilograms / square meter (kg / m2). Knee functions were assessed by The Western Ontario and McMaster Universities Osteoarthritis score (WOMAC). WOMAC index is compromised of 24 parameters that include pain (score range: 0–20), stiffness (score range: 0–8), and functional impairment (score range: 0–68) [10]. The Knee Injury and Osteoarthritis Outcome Score (KOOS) was assessed in all patients with pain, symptoms, activities of daily living, sport and recreation function, and knee-related quality of life [11].

All analysis was performed in the hematology and biochemistry laboratory of our hospital with the use of an ADVIA Centaur CP Immunoassay System (SIEMENS). The following reference ranges were used for serum vitamin D, calcium, vitamin B12, and phosphorus levels. (Vitamin D [9,5-39,6 ng / mL] , Calcium [8,2-10,2 mg / dL], Vitamin B12 [210-915 pg / mL] and Phosphorus [2,5-5 mg / dL]) .

Statistical Analysis

Data analysis was performed by using SPSS for Windows, version 22 (SPSS Inc., Chicago, IL, United States). Data were shown as mean (95% Confidence Interval) where applicable. The mean differences between groups were compared by Student's t-test. Nominal data were analyzed by Pearson's chi-square test. Patients with late OA according to the K & L scale were divided into early stage (stage 0, 1 and 2) and late stage (stage 3 and 4) OA.Patients were divided into three groups according to BMD as follows: osteoporosis, osteopenia and normally. Variables between male and female early and late OA groups were assessed by one-way ANOVA. Multiple Logistic Regression Analyses were applied for calculating odds ratios and 95% confidence intervals for association between age, laboratory parameters with WOMAC index in female and male OA patients separately. A p-value less than 0.05 was considered statistically significant.

Results

Two hundred and seventy-seven osteoarthritis patients were included in the study. One hundred and forty-twowere female and 135 were male. The baseline anthropometric and biochemical characteristics for female and male OA patients are given in Table 1.Male and female OA groups were homogenized with age and BMI. WOMAC index and KOOS score were not different in female and male OA patients.The distribution ratios of OA stages were homogeneous in the groups. Rates of osteoporosis and osteopenia were not different among men and women OA groups.

Vitamin D levels were 12.57 ± 0.57 ng / ml in female OA patients and 15.18 ± 7.34 ng / ml in male OA patients. Vitamin D levels were statistically significantly lower in female OA than in male OA group (p = 0.025) (Figure 1). Calcium and phosphorus

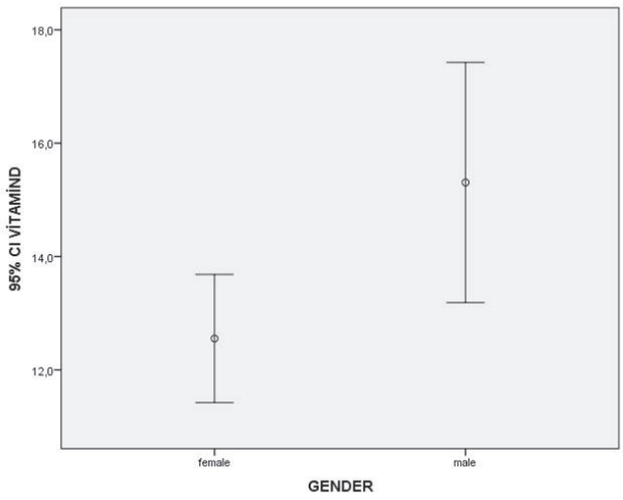

Figure 1. Vitamin D level chart in female and male OA patients

levels were 8.811 ± 0.05 mg / dl, 8,52 ± 0,18 mg / dl in female OA patients and 3,49 ± 0,09 mg / dl, 2,90 ± 0,81 mg / dl in male OA patients, respectively. Calcium and phosphorus levels were significantly higher in female OA patients than in male OA group (p = 0.045 and p = 0.001) (Table 1).

Table 1. Clinical, anthropometric and laboratory features in female and male OA patients

		FEMALE n=142	MALE n=135	p- value
Age (year)		58,82 ±10,14	61,50 ± 11,34	0,122
BMI (kg/m^2)		29,17 ± 0,46	27,78 ± 0,62	0,111
WOMAC index		53,63 ± 1,50	54,52 ± 2,65	0,767
KOOS score		84,01 ± 3,32	82,08 ± 5,41	0,765
Calcium (mg/dl)		8,811 ± 0,05	8,52 ± 0,18	0,045
Phosphorus (mg/dl)		3,49 ± 0,09	2,90 ± 0,81	0,001
Vitamin B12 (pg/ml)		336,91 ± 20,50	334,42 ± 22,26	0,946
Vitamin D (ng/mL)		12,57 ± 0,57	15,18 ± 7,34	0,025
BMD	< 1,5	33 (32%)	41 (30,37%)	0,821
	1,5- 2,49	27 (26,2%)	43 (31,85%)	
	≥ 2,5	43 (41,7%)	51 (37,77%)	

BMI; body mass index, WOMAC index; The Western Ontario and McMaster Universities Osteoarthritis scoreKOOS score; The Knee Injury and Osteoarthritis Outcome Score BMD; bone mineral density. p value; statistical significance <0,005.

We looked at anthropogenic and laboratory characteristics between early and late stage OA patients with osteoporosis, osteopenia, and normal BMD. The age was significantly higher of osteoporosis early-stage and late-stage women OA patients than normal BMD and osteopenia (p <0.001 and p = 0.004, respectively) (Table 2). There was no difference between vitamin D, vitamin B12, calcium, phosphorus, WOMAC index and KOOS scores in early and late stage OA patients with osteoporosis, osteopenia, and normal BMD (Table 2).

WOMAC index was significantly higher in male patients with osteoporosis early stage and late stage OA than patients with osteopenia and normal BMD (p = 0.011 and p = 0.039, respectively) (Table 3). Age, D vitamin, B12 vitamin, calcium, phosphorus, and KOOS scores were not different in early and late-stage OA patients with osteoporosis, osteopenia and BMD normal (Table3).

Multiple regression analysis was performed to evaluate the relationship between knee function score (WOMAC index) and variables in male and female OA patients. The age odds ratio (OR) was 1,047 (95% CI = 1,009-1,086) in female OA patients, and OR was 1.090 (95% CI = 1,021-1,163) in male OA patients. The older age was statistically associated with the WOMAC index in the male and female OA groups. (p=0,014 and p=0,009, respectively) (Table 4).

Discussion

Knee OA is particularly common in elderly people and currently there is no therapy that can slow its progression. At the same time, osteoporosis, which leads to decreased bone mineral density (BMD), degraded micro-architecture of the bone and fragile bones, affects both men and women, but the main burden of the disease is widespread in postmenopausal women [12]. Both diseases are a major cause of morbidity in the elderly population. The relationship between OA and BMD is complex, conflicting and bone metabolism plays a role in the pathophysiology of both Studies have shown thatrisk of OA is reduced in patients with high BMD [13, 14]. In the Rotterdam Study, increased bone mineral density in the femur neck has been shown not to be different in BMD levels in the femur neck, nor in bone loss in the normal group of men with knee osteoarthritis [15]. Lethbridge-Cejku et al. have shown that there is no difference in proximal femur BMD in relation to any radiological changes in the wom-

Table 2. Anthropological, clinical and laboratory features of early stage OA and late stage OA patients with osteoporosis, osteopenia and normal BMD.

	Early Stage Female OA					Late Stage Female OA				
	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P value **	P value*	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P value **	P value*
Age (year)	57,50 ± 2,42	52,40 ± 0,95	49,60 ± 0,89	P(ab)=0,03 P(ac)<0,01 P(bc)=ns	<0,001	69,83 ± 1,30	63,60 ±1,43	63,36 ± 2,26	P(ab)=0,003 P(ac)=0,009 P(bc)=ns	0,004
Vitamin D (ng/mL)	14,78 ± 2,12	12,25 ± 1,14	12,12 ± 1,15	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	12,98 ± 1,56	12,39 ± 1,24	11,57 ± 1,56	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Womac index	42,79 ± 3,95	45,76 ± 2,92	44,17± 2,14	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	58,10 ± 2,94	67,60 ± 3,36	68 ± 4,24	P(ab)=0,036 P(ac)=ns P(bc)=ns	Ns
Koos skoru	54 ± 4,84	59 ± 3,72	48,06 ± 2,71	P(ab)=ns P(ac)=ns P(bc)=0,09	Ns	116,66 ± 5,79	121,64 ± 4,51	113, 79 ± 6,67	P(ab)=ns P(ac)=ns P(bc)=ns	Ns

BMI; body mass index, WOMAC index; The Western Ontario and McMaster Universities Osteoarthritis score KOOS score; The Knee Injury and Osteoarthritis Outcome Score BMD; bone mineral density. p value; statistical significance < 0.005. p value *; with in group, P value**; between groups, Ns; non-significant.

Table 3. Anthropological, clinical and laboratory features of early stage OA and Late Stage OA male patients with osteoporosis, osteopenia and normal BMD

	Early Stage Male OA					Late Stage Male OA				
	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P value **	P value*	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P value**	P value*
Age (year)	59 ± 2,64	52,42 ± 2,07	53,10 ±2,83	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	69 ± 3,73	69 ± 1,72	68,75 ± 5,97	P(ab)=ns P(ac)=ns P(bc)=ns	Ns
Vitamin D (ng/mL)	12,36 ± 2,85	15,25 ±2,22	15,61 ± 2,41	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	14,22 ± 2,34	18,10 ± 2,32	9,67 ± 1,91	P(ab)=ns P(ac)=ns P(bc)=ns	Ns
Womac index	55,67 ±11,9	49,83 ±3,96	35 ± 1,68	P(ab)=ns P(ac)=0,016 P(bc)=0,009	0,011	78,43± 3,86	59,62 ± 4,89	57 ± 8,39	P(ab)=0,019 P(ac)=0,042 P(bc)=ns	0,039
Koos skoru	55 ± 18,24	49,75 ± 4,41	51,50 ± 7,39	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	114 ± 12,38	112,23 ± 6,42	100 ± 13,62	P(ab)=ns P(ac)=ns P(bc)=ns	Ns

BMI; body mass index, WOMAC index; The Western Ontario and McMaster Universities Osteoarthritis score, KOOS score; The Knee Injury and Osteoarthritis Outcome Score BMD; bone mineral density. p value; statistical significance < 0.005. p value *; with in group, P value**; between groups, Ns; non-significant

Table 4. Multivariate regression analysis to determine the factors associated with WOMAC index in male and female OA patients.

	Female		Male	
	AUC (95%CI)	p value	AUC (95%CI)	p value
Age (year)	1,047 (1,009-1,086)	0,014	1,090 (1,021-1,163)	0,009
Vitamin D (ng/mL)	1,023 (0,973-1,077)	0,375	1,032 (0,951-1,119)	0,455
Osteoporosis	1,182 (0,499-2,799)	0,703	0,625 (0,155-2,523)	0,509
Osteopenia	0,724 (0,305-1,715)	0,463	0,212 (0,037-1,211)	0,081

WOMAC index; The Western Ontario and McMaster Universities Osteoarthritis score.

en and man's knee OA [16].

D vitamins are important factors for bone remodeling and bone metabolism [17]. Breijawi and et al. detected a high prevalence of vitamin D deficiency, independent of the BMD [18]. It was shown that vitamin D stimulates synthesis of proteoglycan by mature articular cartilage in vitro [19]; and this suggests that vitamin D may directly affect articular cartilage metabolism. In our study, we found that vitamin D levels were significantly lower in females than in males and in older OA patients with low serum vitamin D levels. Also, there was no difference between vitamin D and calcium levels in osteoporosis and osteopenia groups of women with early and late- stage osteoarthritis. Only late-stage OA patients were older than the early stage OA. Karina et al. reported that vitamin D levels in OA patients who underwent knee arthroplasty were not associated with OA progression. At the same time, they have shown that there is no relationship between T scores and OA stages [20]. Hunter et al. reported that there was no significant relationship between vitamin D levels and osteophytes in the knee [21]. Arden et al. have stated that vitamin D supplementation has no role in knee OA management [22]. Felson et al. have shown that vitamin D levels are not associated with changes in joint space or risk of cartilage loss in patients with knee OA [23]. Ding et al. reported that exposure to sunlight and serum 25 (OH) D levels were associated with decreased knee cartilage loss [24]. In our study, we determined WOMAC index was higher in the osteoporosis group than in the osteopenia group in both early stage and late stage male OA patients, but we could not find any difference between vitamin D levels. The results of the studieshaveshown that low D vitamin level is associated with OA progression and osteoporosis development, but the relationship between OA and vitamin D deficiency is not clear [25]. Divya et al. gave vitamin D supplementation to the patients with 107 knee OA with vitaminD level ≤ 50 nmol / L and after 12 months showed a decrease in knee pain and improved knee function compared to the placebo group [26]. Muraki et al. have stated that vitamin D may be associated with pain and not with radiographic changes in OA [27]. It is known that age, female sex, and physical demand were associated with knee pain [28-31] and radiographic knee OA [32]. When we evaluated the effective factors for the knee function score in our study, we found that only the age factor was the cause of change inmales and females.

Conclusion

After all, the high WOMAC index of late OA patients may cause restraint in movements and decrease in systemic BMD, and D-vitamin supplementation may be said increase BMD, slow down the progression of osteoporosis, reduce pain, but have no effect on OA progression and knee function scores. The sample size is the limitation of our current study.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study 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. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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