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Original Article

Relationship analysis of 25-Hydroxy-vitamin-D and parathyroid hormone in bone mineral density from senile osteoporotic fracture patients

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Abstract: This study aimed to analyze the relationship between 25-Hydroxy-vitamin-D [25(OH)D] and parathyroid hormone (PTH) with bone mineral density (BMD) in senile osteoporotic fracture. The patients suffered from senile osteoporotic fracture and healthy volunteers were enrolled. Serum 25(OH)D and PTH levels were tested by ELISA. BMD at lumbar 1-4, hip joint, and femoral neck was detected by X-ray absorptiometry. The relationship between 25(OH)D and PTH with BMD was analyzed. Serum 25(OH)D level was lower, while PTH level was higher in experimental group compared with control. BMD at lumbar 1-4, hip joint, and femoral neck was significantly lower in experimental group than the control ($P < 0.05$). There were 28% patients suffered from severe 25(OH)D deficiency, 32% patients in 25(OH)D deficiency, 23% in 25(OH)D insufficiency, and 17% in 25(OH)D sufficiency. PTH level gradually declined, whereas BMD at lumbar 1-4, hip joint, and femoral neck gradually elevated following 25(OH)D deficiency improvement ($P < 0.05$). Serum 25(OH)D reduced, while BMD at lumbar 1-4, hip joint, and femoral neck declined in patients with PTH upregulation ($P < 0.05$). Serum 25(OH)D showed positive correlation with BMD at lumbar 1-4, hip joint, and femoral neck ($P < 0.05$). PTH presented no statistical correlation with serum 25(OH)D and BMD ($P > 0.05$). Serum 25(OH)D deficiency and PTH elevation appeared in senile osteoporotic fracture. 25(OH)D was positively correlated with BMD. PTH exhibited no correlation with 25(OH)D or BMD.

Keywords: 25(OH)D, PTH, fracture, BMD

Introduction

In recent years, senile osteoporotic fracture gradually increases following aging of population. There are more than two hundred million patients suffered from osteoporosis, leading to the elevation of fracture [1]. Osteoporosis is featured as low bone mass and bone structure destruction, leading to the increase of bone fragility and fracture. It belongs to the systemic metabolic bone disease that mainly occurs in the spine, proximal femur, and distal radius [2]. The most serious complication of osteoporosis is fracture, which is most common in spine. The fatality rate and disability rate were both high in medulla fracture. Osteoporosis also causes serious influence on self-care ability and brings heavy economic burden to the society and family. Osteoporosis can be divided into primary and secondary [3]. Vitamin D deficiency has become a global problem especially in elderly patients [4]. Vitamin D plays an important role in promoting bone growth and development. Monitoring vitamin D level is of great significance for osteoporosis prevention. 25-Hydroxy-vitamin-D [25(OH)D] is considered as the best indicator to evaluate vitamin D level [5, 6]. Food and Drug Administration confirmed that serum 25(OH)D is an effective index to test vitamin D level. PTH is closely related to 25(OH)D that can be used to assess bone metabolism. PTH is a single chain polypeptide containing 84 amino acids secreted by parathyroid gland. It is an important protein in regulating calcium and phosphorus metabolic balance, and bone transformation [7]. However, there is still unclear about the relationship among serum 25(OH)D, PTH, and bone mineral density (BMD) in senile osteoporotic fracture. This study selected senile osteoporotic fracture patients to analyze the correlation relationship among 25(OH)D, PTH, and BMD.

Table 1. Serum 25(OH)D, PTH, and BMD levels comparison between two groups

Group	Cases	25(OH)D (ng/ml)	PTH (pg/ml)	BMD (g/m^2)		
				Lumbar 1-4	Hip joint	Femoral neck
Experimental group	50	12.34 ± 3.57*	62.08 ± 2.07*	0.801 ± 0.01*	0.807 ± 0.02*	0.801 ± 0.03*
Control	50	18.57 ± 7.95	54.68 ± 15.97	0.877 ± 0.13	0.894 ± 0.17	0.891 ± 0.018

*P < 0.05, compared with control.

Table 2. PTH level and BMD changes in patients with different degrees of 25(OH)D deficiency

Group	Cases	PTH (pg/ml)	BMD (g/m^2)		
			Lumbar 1-4	Hip joint	Femoral neck
Severe deficiency	28	70.79 ± 4.13*,#,&	0.67 ± 0.08*,#,&	0.68 ± 0.07*,#,&	0.62 ± 0.07*,#,&
Deficiency	32	65.33 ± 3.02	0.75 ± 0.09	0.74 ± 0.08	0.72 ± 0.06
Insufficiency	23	59.87 ± 2.46	0.83 ± 0.12	0.86 ± 0.04	0.89 ± 0.11
Sufficiency	17	50.23 ± 1.02	0.97 ± 0.05	0.96 ± 0.05	0.96 ± 0.08

*P < 0.05, compared with deficiency; #P < 0.05, compared with insufficiency; &P < 0.05, compared with sufficiency.

Table 3. 25(OH)D level and BMD changes in patients with different PTH degrees

Group	Cases	25(OH)D (ng/ml)	BMD (g/m^2)		
			Lumbar 1-4	Hip joint	Femoral neck
Elevation	68	9.78 ± 1.57*	0.79 ± 0.02	0.82 ± 0.01	0.81 ± 0.07
Normal	32	15.94 ± 4.03	0.80 ± 0.04	0.83 ± 0.05	0.82 ± 0.06

*P < 0.05, compared with normal control.

Materials and methods

General information

A total of 50 senile osteoporotic fracture patients in people's hospital of Ningxia Hui Nationality Autonomous Region between Jan 2016 and Jan 2017 were enrolled. The patients were diagnosed by CT or MRT, including 27 males and 23 females with mean age at 63.6 ± 1.5 (60-75) years old. Another 50 contemporaneous healthy volunteers were selected as control, including 28 males and 22 females with average age at 65.1 ± 1.5 (60-75) years old. No statistical difference was observed on gender and age between two groups (P > 0.05).

The study protocol was approved by the Research Ethics Committee of people's hospital of Ningxia Hui Nationality Autonomous Region, and all patients gave their informed consent before study commencement.

Exclusion criteria

Previous treatment by drugs that can affect bone metabolism, including diphosphonate, activated vitamin D, calcitonin, and estrogen receptor regulator; hypo- or hyperthyroidism; deformans osteitisj; osteogenesis imperfecta; osteomalacia; Cushing's syndrome; chronic liver disease; chronic obstructive pulmonary disease; chronic kidney disease with serum creatinine level > 177 mol/L; rheumatism and rheumatoid arthritis; application of drugs that influence bone metabolism, including steroid hormones or anticonvulsants for longer than 6 months; gastric ulcer, Crohn's disease, segmental small enteritis, and chronic diarrhea within two years; BMD affected by non-genetic nerve or muscle diseases; limbs activity affected by cardio-cerebral diseases sequela; malignant tumor; premature menopause (< 40 years old); skin disease cannot accept sunlight.

Experimental methods

A total of 4 ml fasting venous blood was extracted and centrifuged at 1700 r/min and 4°C for 10 min. The supernatant was moved to a new Ep tube and further centrifuged at 10,000 r/min for 10 min. At last, the supernatant was stored at -20°C.

ELISA

Serum 25(OH)D and PTH levels were tested by ELISA. The standard sample was diluted and added to the plate for five replicates. After sam-

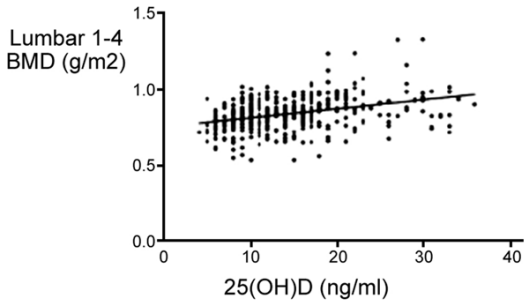

Figure 1. The relationship between 25(OH)D and BMD at lumbar 1-4.

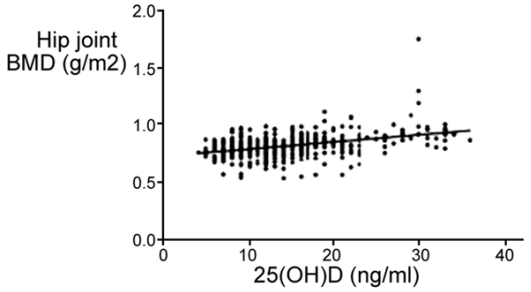

Figure 2. The relationship between 25(OH)D and BMD at hip joint.

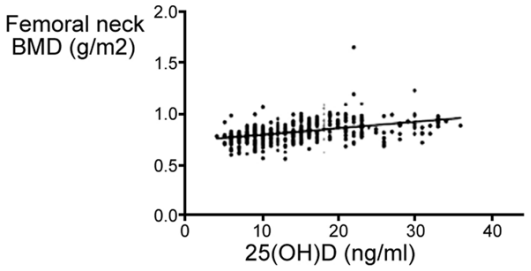

Figure 3. The relationship between 25(OH)D and BMD at femoral neck.

pling, washing, developing, and stopping, the plate was tested at 450 nm on microplate reader to calculate sample concentration.

BMD determination

BMD at lumbar 1-4, hip joint, and left femoral neck was detected by X-ray absorptiometry (GE) to calculate T score.

Judgement standard

Serum 25(OH)D level was used to assess vitamin D state [8]. < 10 ng/mL was severe vitamin D deficiency, ≥ 10 ng/mL and < 20 ng/mL were vitamin D deficiency, ≥ 20 ng/mL and < 30 ng/mL were vitamin D insufficiency; ≥ 30 ng/mL was vitamin D sufficiency. The patients were divided into severe deficiency, deficiency, insufficiency, and sufficiency groups according to the criteria.

Serum PTH level was used to evaluate parathyroid hormone state [9]. < 8.3 pg/mL was insufficiency, ≥ 8.3 pg/mL and < 68 pg/mL were normal, > 68 pg/mL was high. Osteoporosis was diagnosed and classified according to WHO, T score ≤ -2.5 was osteoporosis, T score between -1 and -2.5 was osteopenia, T score > -1 was normal. The patients were divided into three groups according to T score, including osteoporosis group, osteopenia group, and normal control.

Statistical analysis

All data analyses were performed on SPSS 17.0 software. Enumeration data were tested by chi-square test. Measurement data were presented as mean ± standard deviation and compared by ANOVA. Logistic regression model was applied for multivariate analysis. $P < 0.05$ was considered as statistical significance.

Results

Serum 25(OH)D, PTH, and BMD levels comparison between two groups

Serum 25(OH)D, PTH, BMD levels were tested in two groups. Serum 25(OH)D level was lower, while PTH level was higher in experimental group compared with control. BMD at lumbar 1-4, hip joint, and femoral neck was significantly lower in experimental group than the control ($P < 0.05$) (**Table 1**).

PTH level and BMD changes in patients with different degrees of 25(OH)D deficiency

There were 28 patients suffered from severe 25(OH)D deficiency (28%), 32 patients in 25(OH)D deficiency (32%), 23 patients in 25(OH)D insufficiency (23%), and 17 cases in 25(OH)D sufficiency (17%). PTH level gradually declined, whereas BMD at lumbar 1-4, hip joint, and femoral neck gradually elevated following 25(OH)D deficiency improvement ($P < 0.05$). BMD showed no statistical difference among different parts from patients with same 25(OH)D degree ($P > 0.05$) (**Table 2**).

25(OH)D level and BMD changes in patients with different PTH degrees

There were 32 patients appeared PTH elevation, accounting for 32%. Serum 25(OH)D significantly reduced in patients with PTH elevation ($P < 0.05$). BMD at lumbar 1-4, hip joint, and femoral neck exhibited no obvious difference in patients with different PTH degree ($P > 0.05$) (**Table 3**).

Correlation analysis of 25(OH)D and PTH levels with BMD at different parts

Serum 25(OH)D showed positive correlation with BMD at lumbar 1-4, hip joint, and femoral neck ($r = -0.355$, $P < 0.05$, $r = -0.367$, $P < 0.05$, $r = -0.412$, $P < 0.05$). PTH presented no statistical correlation with serum 25(OH)D and BMD ($P > 0.05$) (**Figures 1-3**).

Discussion

Osteoporosis is a systemic metabolic bone disease characterized by low bone mass and bone microstructure damage. Osteoporosis patients can appear increased bone fragility and prone to fracture [10]. One of the risk factors of osteoporosis is vitamin D deficiency. The decrease of sunshine duration in daily life and the use of ultraviolet protective equipment lead to vitamin D deficiency become a global problem. The source of vitamin D includes sunlight that makes skin to produce vitamin D3, and food intake of vitamin D2 that can form 25(OH)D3 and 25(OH)D2 after treated by 25 hydroxylase in the liver. Moreover, they can form 1,25(OH)2D3 and 1,25(OH)2D2 under the effect of 1α hydroxylase in the kidney [11]. 1,25(OH)2D3 is the highest concentration metabolites of vitamin D with half-life at 2~3 weeks. It is not subject to the regulation of calcium, phosphorus, and PTH [12].

In this study, we selected senile osteoporotic fracture patients as experimental group and healthy volunteers as normal control to compare serum 25(OH)D, PTH, and BMD levels. Serum 25(OH)D level was lower, while PTH level was higher in experimental group compared with control. BMD at lumbar 1-4, hip joint, and femoral neck was significantly lower in experimental group than the control. It indicated that serum 25(OH)D level reduced, PTH overexpressed, and BMD declined in senile osteoporotic fracture.

It was found that vitamin D is not only involved in bone metabolism, and also can maintain muscle strength and regulate immune response [13]. This study further compared PTH level in patients with different serum 25(OH)D degrees. PTH level gradually declined, whereas BMD at lumbar 1-4, hip joint, and femoral neck gradually elevated following 25(OH)D deficiency improvement ($P < 0.05$). BMD was lowest in patients suffered from severe 25(OH)D deficiency. It revealed that PTH upregulated, while BMD declined in patients with severe 25(OH)D deficiency. Saadi HF suggested that the risk of hip fracture increased when serum 25(OH)D < 19 ng/mL in female [14]. Gutiérrez OM found that the risk of hip fracture elevated when serum 25(OH)D < 25 ng/mL in old people [15]. Stein MS indicated that the serum 25(OH)D level was low in fall down elder people, which was in accordance with our results [16].

This study further compared serum 25(OH)D level in patients at different PTH levels. 25(OH)D level significantly declined, while BMD exhibited no obvious changes in patients with increased PTH level. PTH shows dual-directional regulation. Sustained PTH stimulus increases bone conversion rate and reduce bone mass, leading to osteoporosis. On the contrary, small dose and intermittent PTH stimulus can promote bone formation [17]. Vitamin D deficiency may induce serum PTH elevation, enhance bone conversion, and accelerate bone loss. Nevertheless, it may attenuate lower limb muscle strength, thus increase the risk of fall down and fracture [18].

This study analyzed the relationship among 25(OH)D, PTH, and BMD at different parts. Serum 25(OH)D showed positive correlation with BMD at lumbar 1-4, hip joint, and femoral neck. PTH presented no statistical correlation with serum 25(OH)D and BMD. Bischoff-Ferrari HA confirmed that serum 25(OH)D level was related to BMD [19]. Nakamura K investigated postmenopausal women and found that serum 25(OH)D showed linear correlation with femoral neck BMD [20]. Cauley reported that 25(OH)D decreased in senile female and increased the risk of fracture [21].

Conclusion

Serum 25(OH)D and BMD reduced, while PTH level elevated in fracture patients. BMD de-

creased in patients suffered from severe serum 25(OH)D deficiency. Serum 25(OH)D was positively correlated with BMD. Fracture prevention should be paid attention in patients with vitamin D deficiency. Positive vitamin D supplement is needed to prevent fall down damage. Osteoporosis should be prevented in patients with elevated PTH level. Meanwhile, serum 25(OH)D and BMD levels should be tested in early stage, which may be helpful to prevent the occurrence and development of osteoporosis.

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Disclosure of conflict of interest

None.

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