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Determining Normal Range of Vitamin D Based on PTH and Bone Mineral Density Changes

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Abstract

PTH is the most important factor which control calcium homeostasis in the body in this study we tried to determine the normal range of PTH and Vitamin D with examining the relation between PTH and bone density and Vitamin D on the base of bones biological changes. Our subjects were, 20 to 69 years-old men and women of Tehran. Serum volume of PTH and vitamin D in different decades of life had significant difference. Range of serum PTH in osteporotic persons was 29.7-38 pgr/lit (95% SD). This range for non osteporotic persons was 24.33-30.2 pgr/lit. In this study ranges below 18 nmol/lit was considered as severe vitamin D deficiency and 23-36nmol/lit as mild deficiency. So the volume more than 36 nmol/lit volumes was normal range of vitamin D. it seems that biological changes of bones associate more with ranges of vitamin D which causes significant changes in PTH.

Keywords: *Vit D, PTH, Normal ranges, Bone mineral density*

Introduction

PTH is the most important factor in Ca homeostasis in the body. This hormone activates the osteoclasts and reabsorption Ca from bone, increase renal tubular reabsorption and at the end increase changing vitamin D to its active form 1,25 (2OH) colecalsiferol in renal that causing increase Ca uptake from intestine (1,2).

The most important biological activity of vitamin D in skeletal system is increasing intestinal Ca absorption (3, 4).Vitamin D deficiency leads to decreased intestinal Ca absorption from 30% to 15% that causes increased PTH (5). Vitamin D deficiency leads to rickets and osteomalacia associated with secondary hyperparathyroidism (5, 6).This secondary hyperparathyroidism even in mild vitamin D deficiency leads to increased Ca reabsorption of bones and decreased bone density (1). Certainly, each factor that decreased serum Ca level causes secondary hyperparathyroidism. The most important causes of disorder are renal failure and vitamin D deficiency.

Considering Ca and phosphorus metabolism, it seems that the balance between vitamin D and PTH has the most important role in Ca homeostasis and bone changes. Disturbance of this balance usually occur after Vitamin D deficiency that causes increasing PTH secretion which in long term associates with decreasing bone density and osteoporosis. Some studies show that as the age increases, the intake of dietary vitamin D decreases. More over, skin synthesis of this vitamin decreases. These increase the prevalence of vitamin D deficiency in elderly people. On the other hand, renal tissue changes witch dependent on age, reduce converting of vitamin D to its active from, so

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that decreasing intestinal Ca absorption, stimulation of PTH secretion and secondary hyperparathyroidism occur. This phenomenon is one of the most important causes of decreasing bone density in elderly persons and age-dependent bone changes.

Bone changes in women are more severe. After menopause, decrease of bone density in women is 3 times more severe than men. This is related to estrogen level changes in women. In women after menopause, estrogen and sex hormones secretion change. One of the effects of estrogen secretion changes is disturbance of Ca set point and then change of set point of PTH secretion that causes hyperparathyroidism after menopause (3). So, sufficient vit D intake is needed not only for Ca homeostasis and bone synthesis in adolescence, but also for prevention of bone density decrease and osteoporosis during old ages (4).

The relation between PTH and vit D is important in pelvis fracture. It is showed that half of the women with pelvis fracture, had vit D deficiency and 37% of them had increased PTH

In this study, relation between PTH and bone mineral density and vit D was investigated. Also by studding this relation, we tried to determine normal range of PTH and vit D on the base of biological bone changes.

Materials and Methods

Subjects were 20 to 69 years-old men and women of Tehran, Capital of Iran. Persons who had diseases such as rheumatoid arthritis, hyper or hypothyroidism, parathyroidism and adrenal, diabetes mellitus, renal failure, aggressive hepatic failure and every kind of cancers, were excluded.

Also people who had menstrual disorders like beginning of menses after the age 18 years-old, absence of menses, having no menses in during last 3 months, having less than 6 times menses during last year in younger than 40-years-old women, ophorectomy under the age of menopause, infertility, pregnancy or breast feeding during the study, smoking more than 10 cigarettes per day, alcohol consumption more than 5 years, and more than one glass a day, drug addiction, professional exercising, lumbar spinal cord fractures after a simple falling, spinal cord deformity, being bed rest in last 2 weeks after an illness, complete bed rest for 3 mounts, consumption of estrogen, progesterone and primarim in menopaused women or those under gone ophorectomy, taking Ca supplement at least one tablet a day consumption of multivitamin and vitamin D in last 2 weeks and vit D ampol in last 6 mounts, were excluded.

For random selecting, information of all first deliveries in Tehran was collected. Sampling was begun in 50 locations which were selected randomly, then in these locations even numbers were selected, until gathering enough subjects.

Sampling was begun after taking an agreement in winter, and then 10 ml blood was taken from each person in his/her house. Samples were centrifuged and separated in sampling places.

These samples were sent to Endocrine Research Centers laboratory of Tehran University and frozen immediately.

Measurement of 25 (OH) vit D was done with radio immunoassay, by using made in England IDS kit and serum PTH radio immune assay, made in U.S.A Dia-sorin kit.

In recalling phase, invitation letters were given to people and volunteers were referred to bone densitometry section of Endocrine Research Center of Tehran University which is located in Shariati hospital. After taking permission, questionnaires were filled and physical examination like weight and height were measured. Then they were inspected to find if they had bone deformities, muscle tenderness and spinal cord deformities. Cases who and any of these disorders were excluded.

So excluded criteria were evaluated in two stages, 1: when invitation letters were given 2: after referring to bone densitometry.

Evaluation of questionnaire was done in Endocrine and Metabolism Research Center of Tehran University of Medical Sciences. In persons

who had used opaque rays' substances, radioactive substances or drugs containing Ca in last 5 days, bone densitometry was postponed at least 5 days. Bone mineral density was measured by lunar machines in DXA way.

This machine was checked with daily standard and special fan tom regularly. Bone mineral density was measured in lumbar spine (2-4), also in the bottom of femur (neck, trockanter and all of the bone) in the scale of gr/cm^2.

Information was saved and analyzed by SPSS # 11.5.Bilateral *T*-test was used for comparison of means. Relations between variables were assessed by linear regression or logistic regression.

Results

A Total of 1229 people were invited to undergo bone densitometry. 124 cases were excluded because of having one of the excluding criteria. After 3 times calling and face to face following, 830 out of 1105 persons (75.1%) took part in this study. Division of persons who did not participate in this project showed no significant difference in different sex and age groups.

Subjects consisted of 39.2% men and 60.8% women. Characteristics of subjects are shown in Table 1. Mean of age had no significant difference between two groups.

Body mass index in women was higher than men. Mean of serum vitamin D in men was lower than women. Variance analysis which was done on serum vitamin D and PTH volume in different decades of life had significant difference (P= 0.001).

In linear regression model, age, sex and PTH had correlation with vitamin D changes (P<0.014). Relation between PTH and vitamin D is shown in Fig. 10.

Linear regression was only significant between PTH and bone density of lumbar spinal cord in women older than 45, but for pelvis bone mineral density, this relationship was not significant. Also in regression analysis bone mineral density in lumbar spinal cord was related to PTH.

Range of PTH in osteoporotic persons was 29.7 to 38 pgr/ lit (95% SD).

This range in non osteoporotic persons was 24.33 to 30.2 pgr/ lit (Fig. 2).

According to this, the range of vitamin D, based on PTH changes, which can be associated with bone mineral density changes, was determined.

In this study volume below 18 nmol/ lit, considered as severe vitamin D deficiency and 23 to 36 nmol/ lit as mild deficiencies. So volume more than 36 nml/ lit considered as normal.

Severe vitamin D deficiency was seen in 25% of men and 45.5% of women, and moderate and mild deficiency in 25.9% and 32% of men and 16.4% and 11.4% of women respectively.

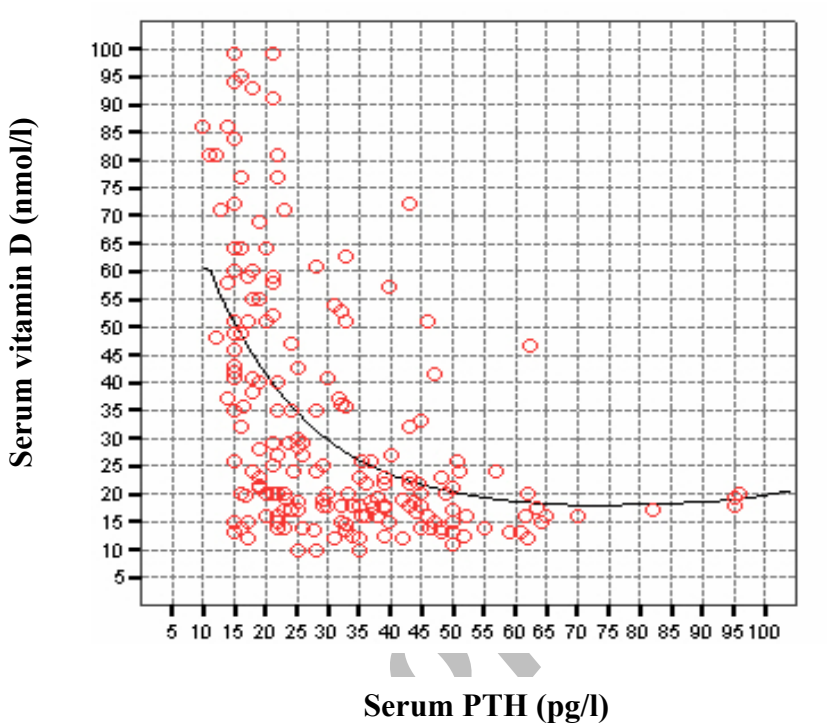
On the whole, 89.2% of men and 73.2% of women had some degrees of vitamin D deficiency and only 17.1% of men and 26.8% of women had normal serum vitamin D volume.

Mean of PTH among subjects who had degrees of vitamin D deficiency showed significant difference in both sexes (P= 0.02).

Table1: demographic characteristics of participants

	Male	Female	p
Age	44.93(±11.79)	43.69(±14.65)	NS
Vitamin D(nmol/l)	29.87(26.3-33.43)	37(32.27-41.88)	0.035
Serum PTH(pg/l)	26.78(24.98-28.57)	31.73(29.78-33.67)	0.001
BMI(kg/m2)	26.2(±4.18)	27.82(±5.45)	0.001

Fig. 1: correlation between vitamin D and PTH



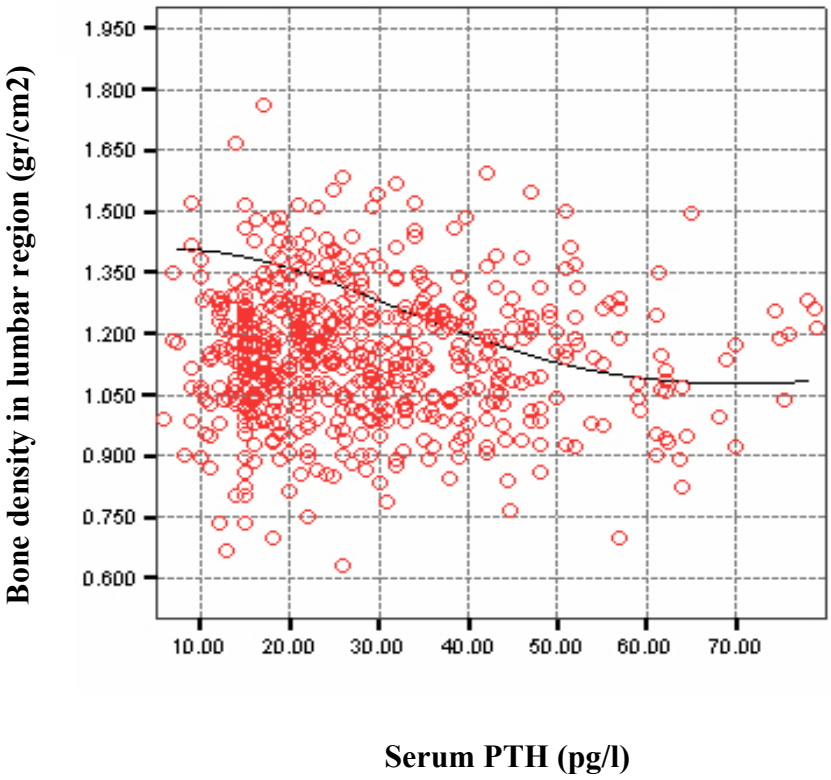


Fig. 2: correlation between bone mineral density and PTH

Discussion

Role of PTH in Ca homeostasis causes close relationship between this hormone and decrease of bone density, osteoporosis and fractures. Results of this study showed that PTH increased as age increased and it accompanied with decrease of bone density. It is similar to the result of other studies.

In these studies showed that age increasing not only decreased uptake of vitamin D but also decreased renal synthesis of active form of this vitamin, which caused disorder in intestinal Ca uptake, increase of PTH and at the end, secondary hyper parathyroidism and negative Ca balance and decrease of bone mass (5-7).

Relationship between PTH and bone mineral density was significant only among women after the age of 40, which was similar to the results of other studies.

These studies showed that because estrogen secretion changed after menopause, PTH adjustment with Ca changed. That is one of the reasons of hyperparathyroidism (3). On the other hand, decrease of bone mass was more prevalent in women than men and prevalence of secondary hyper parathyroidism in men was lower than women (8).

Most of studies showed relation between serum PTH and osteoporosis which were the same as this study, also relation between this hormone and mineral density in pelvis and osteoporotic fractures, was showed (4, 7).

In this study, effects of increase of PTH on decrease of bone density in lumbar spinal cord was more obvious, but it was not similar to the results of studies, which were done in regions with vitamin D deficiency. These studies showed that increase of PTH because of vitamin D deficiency, decreased the bone density in lumbar spinal cord region.

Also some studies showed that compensation of vitamin D deficiency obviously inhibited the decrease of bone density in this area (9, 10). For determining normal range of vitamin D, like most of the other biological parameters, 5 and 95 percentiles were used.

According to this, normal range of vitamin D was reported 25 to 125 nmol/ lit in different studies. Use of this method for determining normal range causes different volumes in different studies. Some of the studies showed that a lot of elderly people who seems healthy with normal vitamin D volume, had increased PTH, so increased bone reabsorption and osteoporosis (7).

Also some studies showed that if vitamin D supplement was given to persons with serum vitamin D volume of, 25 to 50 nmol/lit, PTH volumes would decrease obviously (11).

In some other studies threshold of vitamin D for PTH changes, is reported about 30-77 nmol/lit.

On the whole, it seems that compared to ranges, determined base on percentile in society, ranges of vitamin D which causes significant changes in PTH have more association with biological bone changes (12-16).

On the other hand, in order to evaluating the ranges of PTH changes, which cause significant bone changes, determining normal range of this hormone based on bone changes is necessary.

So in this study, normal range of vitamin D was determined, base on significant changes of PTH which associated with biological bone changes.

References

1. Dawson-Hughes B, Harris S, Dallal GE (1991). Serum ionized calcium, as well as phosphorus and PTH, is associated with plasma 1, 25-dinydroxy vitamin D3 concentration in normal postmenopausal women. *J Bone Miner Res*, 6: 461-68.
2. Weinstein RS, Underwood JL, Hutson MS, Deluca HF (1984). Bone histoplasmorphometry in vitamin D deficient rats infused with calcium and phosphorus. *AMJ physiol*, 246: E499.
3. Konis J (1994). *Osteoporosis*, Black well science, 56-62.

4. LeBoff MS, Kohlmeier L, Hurwitz S. (1999) Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA*, 281: 1595.
5. Gallagher JC, Riggs BL, Eisman J (1979). Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients: Effect of age and dietary calcium. *J Clin Inves*, 64: 729.
6. Riggs BL, Nelson KI (1985). Effect of long term treatment with calcitriol on calcium absorption ams mineral metabolism in postmenopausal osteoporosis. *J Clin Endocrinol Metab*, 61: 457.
7. Akesson K, Lau L-HW, Baylink DJ (1997). Rational for active vitamin D analog therapy in senile osteoporosis. *Calcif Tissue Int*, 60: 100-104.
8. Orwool ES, Oviatt SK, Mcclung MR (1990). The rate of bone mineral loss in normal men and the effects of calcium and cholecaciferol supplementation. *Ann Intern med*; 112: 29.
9. Aaron JE, Gallagher JC, Anderson J (1974). Frequency of osteomalacia and osteoporosis in fracture of the proximal femur. *Lancet*, 1: 229.
10. Villareal DT, Civitelli R, Chines A, Aviolo LV (1991). Subclinical vitamin D deficiency in postmenopausal women with low vertebral bone mass. *J Clin Endocrinol Metab*, 72: 628.
11. Malabanan A, Veronikis IE, Holick MF (1998). Redifining vitamin D insufficiency. *Lancet*; 351(9105): 305-6.
12. Need A, Horowitz M, Morris H (2000). Vitamin D Status: effects on parathyroid hormone and 1, 25-dihydroxyvitamin D in postmenopausal women. *Am J Clin Nurt*, 71(6): 1577-81.
13. Leboff MS, Kohlmeier L, Hurwitz S (1999). Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *JAMA*, 281(16): 1505-11.
14. Harris SS, Soteriades E, Coolidge JA (2000). Vit D insufficiency and hyperparathyroidism in a low income, multiracial, elderly population. *J Clin Endocrinol Metab*, 85(11): 4125-30.
15. Haden ST, Fuleihan GEH, Angell JE (1999). Calcidiol and PTH levels in women attending on osteoprosis program. *Calcif tissue Res*, 64(4): 275-79.
16. Chapuy MC, Preziosi P, Maamer M (1997). Prevalence of vitamin D insufficiency in on adult normal population. *osteoprosis Int*, 7(5): 439-43.