CEOG Clinical and Experimental Obstetrics & Gynecology

Relevance of parathyroid hormone (PTH), vitamin 25(OH)D3, calcitonin (CT), bone metabolic markers, and bone mass density (BMD) in 860 female cases

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Summary

Objective: To study the relevance of PTH, 25(OH)D3, CT, bone resorption markers C-terminal telopeptide of type I (CTX-1), and tartrate-resistant acid phosphatase (TRACP), bone formation markers bone gla protein (BGP), bone alkaline phosphatase (BALP) with the femoral neck BMD in females. *Materials and Methods:* PTH, 25(OH)D3, CT, CTX-1, TRACP, BGP, and BALP were detected by an enzyme immunoassay analyzer and femoral neck BMD were measured by a BMD detector. The results of 860 females were divided into several groups according to standard of five-year age intervals. SPSS 13.0 software was used for statistical analysis. *Results:* The measured values of PTH, 25(OH) D3 and CT had no differences in 35-50 age group. The measured values of 25(OH) D3 began to decline after the age of 50, and 25(OH)D3 had positive relevance with BMD. The values of CT were decreased in the age groups from 65 to 79 years old, and were significant positive correlated with BMD. The CTX-1 and TRACP had negative relevance with BMD in 35-45 age group and BGP and BALP had positive relevance with BMD in 35-45 age group. The BGP, BALP increased significantly in 50-60 age group, and CTX-1, TRACP, BGP, and BALP had negative relevance with BMD in 50-60 age group. BGP and BALP began to decline and had positive relevance with BMD after the age of 65, and CTX-1 and TRACP had negative relevance with BMD after the age of 65. *Conclusions:* PTH, 25(OH)D3, CT, CTX-1, TRACP, BGP, and BALP were the important technical means for monitoring the level of bone metabolism and the diagnosis and differential diagnosis of osteoporosis.

Key words: calcium and phosphorus metabolism regulation indicators, bone metabolism markers, femoral neck BMD, relevance

Introduction

Osteoporosis is a multifactorial polygenic disease, associated with low systemic bone mass, bone structure damage, reduced bone strength, and increased fracture risk [1]. Basic life activities of bone tissue are the process of bone remodeling, including bone resorption and bone formation. Bone remodeling accompanied during a person's life, with osteoclasts and osteoblasts together complete the update process of bone tissue, that is, bone degradation and an equal amount of new bone to replace [2, 3]. Bone remodeling is in a dynamic equilibrium under normal circumstances. When bone resorption is greater than bone formation, osteopenia or even osteoporosis will occur. Bone remodeling is affected by many hormones, cellular and humoral factors, and cell metabolites. These hormones and factors play a role in bone metabolic regulation through the promotion or suppression of the development of osteoblasts and osteoclasts, and enhance or inhibit the activity of osteoblasts and osteoclast [4].

At present, domestic and international studies have shown that osteoblasts and osteoclasts metabolic product, cytokines and humoral factors, and bone metabolism regulating hormones can be detected by biochemical detection technique. Previous domestic and international studies have reported the research result of different races, different ages, and different regions of bone metabolism markers [5-7], but are insufficient study indicators, due to the small sample size and the lack of a comparative study of the different age groups. In this study, the relevance of PTH, 25 (OH) D3, CT, CTX-1, TRACP, BGP, and BALP with the femoral neck BMD in females 35-79 years of age of Han nationality from Changchun were researched, and the correlation of bone metabolism markers in 860 cases of women of different age groups with bone mineral density were analysed. The authors' purpose is to investigate the laws of bone metabolism markers and BMD changes and to prove its significance in the diagnosis of osteoporosis.

Materials and Methods

Subjects

The study included 860 cases of 35 to79-year-old Han women in Jilin Province, including teachers, workers, cadres, service industry workers, and retired. Acute and chronic liver and kidney disease, diabetes, hyperparathyroidism, hypothyroidism, hyperthyroidism, hypothyroidism, and cancer and chemotherapy and

Revised manuscript accepted for publication August 1, 2013

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLII, n. 2, 2015
doi: 10.12891/ceog1725.2015

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Table 1. — *The measurement results of bone metabolism indicators and BMD in 860 cases of female.*

Age(years)	N	CTX-1(pg/L)	TRACP(ug/L)	BGP(pg/ml)	BALP(pg/ml)	BMD(g/m^2)
35~39	59	0.42±0.36	2.04±1.23	15.01±7.51	14.07±5.42	0.605±0.068
40~44	66	0.39±0.52	2.01±1.14	16.14±7.29	16.07±4.95	0.594±0.056
45~49	72	0.38±0.42	2.09±1.21	15.07±6.75	15.05±6.04	0.591±0.048
50~54	80	0.46±0.41	2.65±1.51	13.57±7.52	17.60±7.85	0.590±0.082
55~59	85	0.71±0.42	3.01±2.54	14.81±5.28	19.65±7.14	0.547±0.082
60~64	90	0.61±0.58	3.00±2.81	11.09±6.05	18.31±8.92	0.512±0.085
65~69	164	0.61±0.59	2.55±2.12	11.00±7.01	16.03±6.41	0.473±0.086
70~74	145	0.61±0.60	2.41±2.07	10.81±6.77	15.68±7.03	0.440±0.079
75~79	73	0.61±0.61	2.32±2.04	10.48±6.54	15.23±5.59	0.417±0.088

Table 2. — *The measurement results of calcium and phosphorus metabolism regulation indicators and BMD in 860 female cases.*

Age (years)	N	PTH (U/l)	25(OH)D3 (μg/ l)	CT (pg/ml)	BMD (g/m^2)
35~39	59	41.72 ± 38.52	57.47 ± 34.72	2.38 ± 1.59	0.605 ± 0.068
40~44	66	42.22 ± 41.50	54.32 ± 42.92	2.40 ± 2.01	0.594 ± 0.056
45~49	72	42.92 ± 46.56	51.23 ± 29.68	2.41 ± 1.57	0.591 ± 0.048
50~54	80	41.29 ± 35.34	46.35 ± 35.26	2.45 ± 1.29	0.590 ± 0.082
55~59	85	47.63 ± 35.96	48.69 ± 35.85	2.62 ± 1.61	0.547 ± 0.082
60~64	90	45.56 ± 40.21	44.86 ± 38.21	2.79 ± 1.35	0.512 ± 0.085
65~69	164	45.23 ± 42.13	44.26 ± 36.72	2.18 ± 1.54	0.473 ± 0.086
70~74	145	46.12 ± 43.15	41.48 ± 36.73	2.14 ± 1.21	0.440 ± 0.079
75~79	73	43.72 ± 35.16	41.26 ± 39.45	2.11 ± 1.29	0.417 ± 0.088

Table 3. — *The study on the relevance of bone metabolism indicators with BMD in females of different age groups.*

Group	Varible	CTX-1 (pg/l)	TRACP (ug/l)	BGP (pg/ml)	BALP (pg/ml)
35-45 age	r	-0.317	-0.261	0.374	0.703
	P	0.012*	0.004*	0.010*	0.000*
50-60 age	r	-0.402	-0.274	-0.307	-0.469
	P	0.016*	0.004*	0.010*	0.020*
After 65 age	r	-0.390	-0.218	0.371	0.698
	P	0.012*	0.004*	0.010*	0.000*

*$p < 0.05$ (the bone metabolism indicators have relevance with BMD in females of different age groups).

Table 4. — *The relevance of calcium and phosphorus metabolism regulation indicators with BMD.*

Variable	PTH(U/l)	25(OH)D$_3$ (μg/l)	CT (pg/ml)
r	-0.455	0.215	0.312
P	0.014*	0.021*	0.001*

*$p < 0.05$ (the calcium and phosphorus metabolism regulation indicators have relevance with BMD).

radiotherapy patients were excluded. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of Jilin University. Written informed consent was obtained from all participants.

Detection method

Enzyme immunoassay analyzer was used to detect PTH, 25 (OH) D3, CT, CTX-1, TRACP, BGP, and BALP, and femoral neck BMD was measured by a bone mineral density detector.

Statistical analysis

SPSS13.0 software was applicated for statistical analysis of calcium and phosphorus metabolism regulation indicators, bone metabolism markers and BMD measurements of 860 cases, the relevance of calcium and phosphorus metabolism regulation indicators, and bone metabolism markers with BMD were analysed using linear correlation analysis. A $p < 0.05$ was considered statistically significant.

Results

The measured values of PTH, 25 (OH) D3, and CT showed no differences in 35-50 age group. The measured values of 25 (OH) D3 began to decline after the age of 50, and 25 (OH) D3 had positive relevance with BMD. The measured values of CT was decreased in the age groups from 65 to 79 years old, and was significant positively correlated with BMD. The CTX-1, TRACP had negative relevance with BMD in 35-45 age group and BGP and BALP had positive relevance with BMD in 35-45 age group. BGP and BALP increased significantly in 50-60 age group, and CTX-1, TRACP, BGP, and BALP had negative relevance with BMD in 50-60 age group. BGP and BALP began to decline and had positive relevance with BMD after the age of 65, and CTX-1 and TRACP had negative relevance with BMD after the age of 65. The results of bone metabolism indicators and BMD of 860 female cases (g/cm^2) are shown in Table 1. The results of calcium and phosphorus metabolism reg-

ulation indicators and BMD of 860 female cases (g/cm^2) are shown in Table 2. The study on the relevance of bone metabolism indicators with BMD in 35-45 age group in female are shown in Table 3. The study on the relevance of bone metabolism indicators with BMD in 50-60 age group are shown in Table 3. The study on the relevance of bone metabolism indicators with BMD after the age of 65 are shown in Table 3. The study on the relevance of calcium and phosphorus metabolism regulation indicators with BMD are shown in Table 4.

Discussion

The body maintains calcium and phosphorus metabolism homeostasis under the fine-tuning of PTH, 25 (OH) D3, and CT.

PTH is a kind of straight-chain polypeptide hormone consisting of 84 amino acids, synthesized and secreted by parathyroid cells. The main role is to increase bone calcium absorption and to reduce urinary calcium excretion. CT is a peptide hormone consisting of 32 amino acids and is secreted by thyroid C cells. Its main role is to inhibit bone resorption, reduce kidney reabsorption of calcium and phosphorus, and lower calcium in blood. 25 (OH) D3 is necessary for absorption of intestinal calcium and phosphorus and bone mineralization. Under physiological conditions, 25 (OH) D3 can stimulate the activity of osteoblasts and promote the formation of bone matrix. Large doses of 25 (OH) D3 are an activating factor of osteoclasts [8]. Studies have shown that the levels of 25 (OH) D3 decreased and the levels of PTH increased when age-related osteoporosis occurred, in order to regulate the metabolism of 25 (OH) D3 [9]. This study showed that the measured values of 25 (OH) D3 significantly decreased in the 65 -79 age group, and had positively correlated with BMD ($p < 0.05$). PTH increased slightly in the same age group, the difference was not significant. The levels of CT reduction appeared in the age of 65 -79 age group, and had positive correlation with BMD ($p < 0.05$). The changes of PTH, 25 (OH) D3, and CT had no differences between the sexes.

CTX-1 and TRACP are important biochemical parameters reflecting bone resorption. The quality of bone is decided by bone microstructure, bone metabolism transformation, the degree of bone mineralization and bone collagen, and bone matrix nature [10]. CTX-1 are specific indicators to reflect the type I collagen decomposition. When the type I collagen structure, content, and stability is abnormal, it will result that bone turnover is accelerated and the peptide fragments of type I collagen are degradated into the blood, the CTX-1 levels in blood can be significantly increased [11]. TRACP is released by osteoclasts, increasing the activity of osteoclasts [12]. The authors' previous studies have shown that BGP and BALP levels of 791 cases of Han population of 50 to 59-year-old females was significantly higher than in males, TRACP and CTX-1 was negatively related with BMD, TRACP and CTX-1 reflects both the status of bone resorption and bone turnover. Obrant *et al.* [13] found that serum TRACP was significantly elevated in women with osteoporotic fractures. This study shows that BMD of 35 to 45-year-old females was higher than the 50 to 79 age group. CTX-1 and TRACP of 50 to 79-year-old females was significantly higher than other age groups of women, was negatively correlated with BMD, and consistent with domestic and foreign reports [11-13].

Bone is metabolism living tissue, osteoclasts continue to absorb old bone, and osteoblasts continue to form new bone bone, jointly completing bone remodeling. BALP and BGP are important biochemical parameters that reflect bone formation. BGP is the most abundant non-collagen protein in the bone tissue, composed of 49 amino acids, its physiological function is to maintain bone mineralization rate, inhibit the formation of the carboxyl apatite crystallization. The Owe Löfman *et al.* [14] found that BGP of 1-15 years postmenopausal women continues to rise and that of 65 to 80-year-olds decreased to a low level. Research has shown that osteocalcin is involved in bone remodeling via a negative feedback mechanism [15]. Serum BALP exists in multiple homodimeric forms, 50% from bone, which is secreted by osteoblast and is closely related with bone formation and bone mineralization [16]. This study shows that BGP and BALP levels of 50 to 64-year-olds was significantly higher than other age groups and negatively with BMD; Gomesz *et al.* [17] reported the same results. The study also showed that the BALP and BGP levels of women after the age of 65 began to decline and reached the same conclusion with Gomesz *et al.* Proven that bone metabolism of 1-15 years postmenopausal women was in a high conversion state, after the age of 65, bone resorption and bone formation were reduced gradually to enter the low conversion state [17, 18].

In summary, jointly using calcium and phosphorus metabolism regulation indicators, bone metabolic markers, and BMD in the diagnosis of osteoporosis is superior than BMD diagnosis independently. PTH, 25 (OH) D3, CT, CTX-1, TRACP, BGP, and BALP have an effect on bone quality via interactive process of bone metabolism, and are important association with BMD, and the basis of molecular biology for the early and differential diagnosess of osteoporosis [9, 19-21]. They not only have an important clinical value on osteoporosis prevention and treatment, but can also be used as important technical means for the evaluation of drug treatment and screening for population at high risk of osteoporosis.

Acknowledgements

This study was Supported by People's Republic of China, Ministry of Civil Affairs, "Eleventh Five-Year" osteoporosis project of gerontology study (Grant No. Minrenjiaoke-2007-18-1).

References

[1] Mengmeng Z., L., Ying L., Xuena P., Binbin L., Liu Z.: "A study of bonemineral density and prevalence of osteoporosis in Chinese people of Han nationality from Changchun". *Arch. Osteoporos.*, 2012, *7*, 31.

[2] Szulc P., Delmas P.D.: "Biochemical markes of bone turnover in men". *Calcif. Tissue Int.*, 2001, *69*, 229.

[3] Epstein S.: "The roles of bone mineral density, bone turnover, and other properties in reducing fracture risk during antiresorptive therapy". *Mayo Clin. Proc.*, 2005, *80*, 379.

[4] Cremers S, Garnero P.: "Biochemical markers of bone turn over in the clinical development of drugs for osteoporosis and metastasis bone disease: potential uses and pitfalls". *Drugs*, 2006, *66*, 2031.

[5] Pi Y.Z., Wu X.P., Liu S.P., Luo X.H., Cao X.Z., Xie H., *et al.*: "Age-related changes in bone biochemical markers and their relationship with bone mineral density in normal Chinese women". *J. Bone Miner. Metab.*, 2006, *24*, 380.

[6] Iki M., Takashi A., Matsumoto T., Nishino H., Kagamimori S., Kagawa Y., *et al.*: "Reference database of biochemical markers of bone turnover for the Japanese female population. Japanese Population-based Osteoporosis (JPOS) Study". *Osteoporos Int.*, 2004, *15*, 981.

[7] Desai M.P., Bhanuprakash K.V., Khatkhatay M.I., Donde U.M.: "Age-related changes in bone turnover markers and ovarian hormones in premenopausal and postmenopausal Indian women". *J. Clin. Lab. Anal.*, 2007, *21*, 55.

[8] Rios-Fernández R., Callejas-Rubio J.L., Fernández-Roldán C., Simeón-Aznar C.P., García-Hernández F., Castillo-García M.J., *et al.*: "Bone mass and vitamin D in patients with systemic sclerosis from two Spanish regions". *Clin. Exp. Rheumatol.*, 2012, *30*, 905.

[9] Bauer D.C., Garnero P., Harrison S.L., Cauley J.A., Eastell R., Ensrud K.E., *et al.*: "Biochemical markers of bone turnover, hip bone loss, and fracture in older men: the MrOS study". *J. Bone. Miner. Res.*, 2009, *24*, 2032.

[10] Nishizawa Y., Ohta H., Miura M., Inaba M., Ichimura S., Shiraki M., *et al.*: "Guidelines for the use of bone metabolic markers in the diagnosis and treatment of osteoporosis (2012 edition)". *J. Bone Miner. Metab.*, 2013, *31*, 1.

[11] Herrmann M., Seibol M.: "The amino and caboxyterminal corss-linked telopeptldes of collagen type I, NTX-I and CTX-I: a comparative review". *Clin. Chim. Acta*, 2008, *393*, 57.

[12] Yamada S., Tsuruya K., Yoshida H., Taniguchi M., Haruyama N., Tanaka S., *et al.*: "The clinical utility of serum tartrate-resistant acid phosphatase 5b in the assessment of bone resorption in patients on peritoneal dialysis". *Clin. Endocrinol.*, 2013, *78*, 844.

[13] Obrant K.J., Ivaska K.K., Gerdhem P., Alatalo S.L., Pettersson K., Väänänen H.K.: "Biochemical markers of bone turnover are influenced by recently sustained fracture". *Bone*, 2005, *36*, 786.

[14] Löfman O., Magnusson P., Toss G., Larsson L.: "Common biochemical markers of bone turnover predict future bone loss: A 5-year follow-up study". *Clin. Chim. Acta*, 2005, *356*, 67.

[15] Ducy P.: "The role of osteocalcin in the endocrine cross-talk between bone remodeling and energy metabolism". *Diabetologia*, 2011, *54*, 1291.

[16] Chailurkit L.O., Suthutvoravut U., Mahachoklertwattana P., Charoenkiatkul S., Rajatanavin R.: "Biochemical markers of bone formation in Thai children and adolescents". *Endocr. Res.*, 2005, *31*, 159.

[17] Gomesz B. Jr., Ardakani S., Ju J., Jenkins D., Cerelli M.J., Daniloff G.Y., *et al.*: "Monoclonal antibody assay for measuring bone-specific alkaline phosphatase activity in serum". *Clin. Chem.*, 1995, *41*, 1560.

[18] Garnero P., Sornay-Rendu E., Claustrar B., Delmas P.D.: "Biochemical markets of bone turnover, endogenous hormones and the risk of fracture in postmenpausal women: the OFELY study". *J. Bone Miner. Res.*, 2000, *15*, 1526.

[19] Olmos J.M., Hernández J.L., Llorca J., Nan D., Valero C., González-Macías J.: "Effects of 25-hydroxyvitamin D3 therapy on bone turnover markers and PTH levels in postmenopausal osteoporotic women treated with alendronate". *J. Clin. Endocrinol. Metab.*, 2012, *97*, 4491.

[20] Hellekson K.L.: "NIH releases statement on osteoporosis prevention, diagnosis, and therapy". *Am. Fam. Physician,* 2002, *66*, 161.

[21] Delmas P.D., Eastell R., Garnero P., Seibel M.J., Stepan J.: "The use of biochemical markers of bone turnover in osteoporosis". *Osteoporos*. Int., 2000, *11*, S2.

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