Bone metabolism is influenced by serum 25-hydroxyvitamin D in healthy children

Czekuc-Kryskiewicz Edyta[1], Karczmarewicz Elzbieta[1], Jaworski Maciej[1], Czech-Kowalska Justyna[2], Gorska Anna[3], Konstantynowicz Jerzy[4], Pludowski Paweł[1], Jarosław Piskorski[5], Lorenc Roman[1]

[1]Department of Radioimmunology, Biochemistry and Experimental Medicine, The Children's Memorial Health Institute, Warsaw, Poland; [2]Neonatal Intensive Care Unit, The Children's Memorial Health Institute, Warsaw, Poland; [3]Department of Family Medicine and Community Nursing, Medical University of Bialystok; [4]Department of Pediatrics and Developmental Disorder, Medical University of Bialystok; [5]Institute of Physics, University of Zielona Gora, Zielona Gora, Poland

Introduction

Vitamin D is important for calcium metabolism and accretion of bone mass during growth (1). In addition to profound effects on bone, vitamin D also has several nonskeletal actions: it modifies immune responses and has antimicrobial properties and may thus influence the development of autoimmune diseases such as type 1 diabetes (2-5). The concentration of 25-hydroxyvitamin D [25(OH)D] in blood is regarded as the best indicator of vitamin D status (6). There is as yet no consensus about the threshold level of 25(OH)D that indicates vitamin D deficiency in children. Biochemical markers of bone remodeling provide a means of evaluating skeletal dynamics that complements static measurement of bone mineral density (7). Only few data exist describing the effects of increasing serum 25(OH)D on bone metabolism markers. In Caucasian adolescent girls, a positive association has been reported between vitamin D status and bone mass measurements (8), whereas other studies did not find this relationship (9).

Aim

The aim of the study was to explore the association between serum 25(OH)D and bone metabolism markers in healthy Polish children.

Patients and methods

Serum levels of bone formation (OC, P1NP) and bone resorption (CTx) markers (Cobas e411, Roche Diagnostics) were determined in 161 healthy children (mean age: 9.47±4.94 years; range: 1.92-19.66). Vitamin D status was evaluated by serum levels of 25(OH)D and PTH (Cobas e411; Roche Diagnostics). Densitometric parameters of total body and spine (L2-L4) bone mineral density (TBBMD, LSBMD; g/cm^2) and mineral content (TBBMC, LSBMC; g) were measured by dual energy X-ray absorptiometry (DXA) [Lunar DPX-L]. The association within different bone metabolism markers was studied with the scatter plot matrix technique and the Pearson correlation coefficient. Bone metabolism markers reference intervals were prepared according to the CLSI 28 A3 guidelines (10). Because of the small sample size, the robust method for reference interval determination was used (10), and the data was partitioned according to the SD1>1.5 SD2 or z>z* rule (10) was applied. To explore the associations between bone metabolism and densitometric status and vitamin D multiple regression analysis was used. Only results with p<0.05 were considered significant.

Results

Anthropometric characteristic of the study group was showed in Table I. Serum 25(OH)D levels <10 ng/ml were described in 25.0% children, 10-20 ng/ml in 40.8% children and >20 ng/ml in 34.2% cases. Only 12.5% patients have serum 25(OH)D >30 ng/ml. Vitamin D status deteriorated with age (Figure 1). Positive correlations were observed among the three bone metabolism markers (OC vs. P1NP: R=0.74, p<0.001; OC vs. CTx: R=0.76, p<0.001; P1NP vs. CTx: R=0.67, p<0.001). The correlation between serum 25(OH)D and PTH (R=-0.26, p=0.002) indicate significant negative association between these parameters. Multivariate analysis for predictors of sex- and age-adjusted bone metabolism markers showed that serum 25(OH)D was strongly and positively associated with OC, P1NP and CTx in healthy children, explaining 10.3% of the variance in OC (p<0.001), 12.5% in P1NP (p<0.0001), and 16.2% in CTx (p<0.0001) (Table II). The effect of PTH on bone metabolism was less evident in our study (Table II). The relationship between 25(OH)D levels and LSBMC and LSBMD was observed (Table III).

Conclusions

Strong and positive association of serum 25(OH)D with bone formation as well as resorption markers indicates that proper vitamin D status is very important for bone health especially in period of bone mass accrual.

Table I. Descriptive characteristic of studied children population

Parameter mean±SD (min-max)	Whole group (N = 161)	Girls (N = 74)	Boys (N = 87)	*p* (F vs. M)
Age (years)	9.5±4.9 (1.9-19.7)	9.2±5.2 (2.9-19.7)	9.7±4.8 (1.9-18.0)	NS
Weight (kg)	42.2±27.1 (11.6-134.5)	38.7±27.3 (11.6-114.0)	45.1±26.7 (13.3-134.5)	NS
Height (cm)	135.7±29.0 (91.9-192.0)	131.3±28.4 (91.9-183.0)	139.5±29.2 (92.5-192.0)	NS
BMI (kg/m^2)	20.26±6.48 (12.38-41.03)	19.58±6.65 (12.38-39.49)	20.84±6.32 (14.03-41.03)	NS
25(OH)D (ng/ml)	17.49±9.88 (2.70-55.70)	19.02±10.67 (3.20-55.70)	16.15±8.97 (2.70-40.34)	NS
PTH (pg/ml)	32.46±12.35 (3.16-67.52)	33.08±13.52 (3.16-67.52)	31.92±11.27 (8.35-57.59)	NS

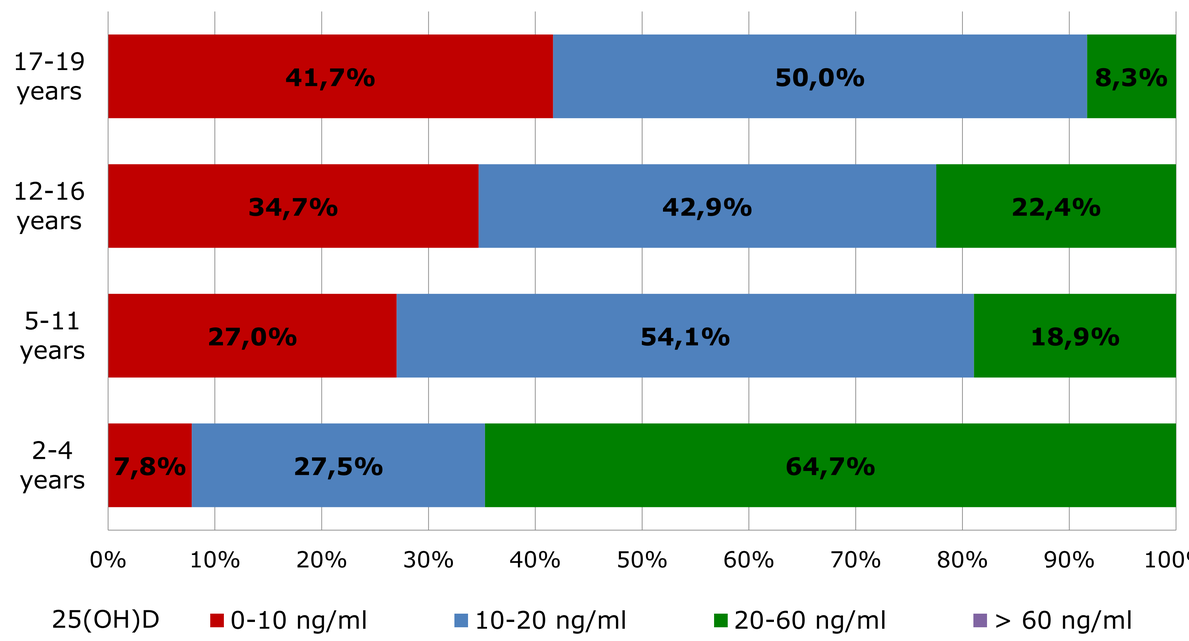

Figure 1. Distribution of 25 (OH) D serum concentrations in different age groups of Polish healthy children

Table II. Multivariate analysis for predictors of sex- and age-adjusted bone metabolism markers

Variables	β[a]	p	Model R^{2b}
OC			**10.3%**
25(OH)D	0.352	< 0.001	**(p < 0.001)**
PTH	0.168	0.02	
P1NP			**12.5%**
25(OH)D	0.925	< 0.001	**(p < 0.0001)**
PTH	0.073	NS	
CTx			**16.2%**
25(OH)D	0.006	< 0.001	**(p < 0.0001)**
PTH	0.002	0.021	

[a] Unstandardized regression coefficient; indicates the difference in the outcome variable (OC, P1NP, CTx) per unit change in the independent variables
[b] The amount of variance in the dependent variable that can be explained by the model

Table III. Multivariate analysis for predictors of sex- and age-adjusted (Z-score) densitometric parameters of bone mass and density

Variables	β[a]	p	Model R^{2b}
Z-score TBBMC			2.7%
25(OH)D	0.006	NS	NS
PTH	0.024	0.03	
Z-score TBBMD			1.8%
25(OH)D	0.008	NS	NS
PTH	0.02	NS (0.052)	
Z-score LSBMC			16.4% (p<0.01)
25(OH)D	0.316	p<0.05	
PTH	0.366	p<0.01	
Z-score LSBMD			14.3% (p<0.05)
25(OH)D	0.189	NS	
PTH	0.389	p<0.005	

[a] Unstandardized regression coefficient; indicates the difference in the outcome variable (TBBMD, TBBMC, LSBMD, LSBMC) per unit change in the independent variables
[b] The amount of variance in the dependent variable that can be explained by the model

Financial support: CMHI Internal Grants: S109/09, 181/07, Ministry of Science and Higher Education Grant 5412/B/P01/2010
Acquiring of Cobas e411 analyzer (Roche Diagnostics) and ultra-low temperature freezers MDF-U500Vx (Sanyo) were co-financed by ERDF (EU Structural Funds) project POIG.02.01.00-14-059/09

1. Lehtonen-Veromaa MK, Mottonen TT, Nuotio IO, et al. (2002) Vitamin D and attainment of peak bone mass among peripubertal Finnish girls: a 3-y prospective study. Am J Clin Nutr 76: 1446-53
2. Brehm JM, Schuemann B, Fuhlbrigge AL, et al. (2010) Serum vitamin D levels and severe asthma exacerbations in the childhood asthma management program study. J Allergy Clin Immunol 126: 52-8
3. Walker VP, Zhang X, Rastegar I, et al. (2011) Cord blood vitamin D status impacts innate immune responses. J Clin Endocrinol Metab 96: 1835-43
4. Urashima M, Segawa T, Okazaki M, et al. (2010) Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren. Am J Clin Nutr 91: 1255-60
5. Hyppönen E, Läärä E, Reunanen A, et al. (2001) Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. Lancet 358: 1500-3
6. Hollis BW. (1996) Assessment of vitamin D nutritional and hormonal status: what to measure and how to do it. Calcif Tissue Int 58: 4-5
7. Looker AC, Bauer DC, Chesnut CH III, et al. (2000) Clinical use of biochemical markers of bone remodeling: current status and future directions. Osteoporos Int 11: 467-80
8. Cashman KD, Hill TR, Cotter AA, et al. (2008). Low vitamin D status adversely affects bone health parameters in adolescents. Am J Clin Nutr 87: 1039-44
9. Willett AM. (2005) Vitamin D status and its relationship with parathyroid hormone and bone mineral status in older adolescents. Proc Nutr Soc 64: 193-203
10. CLSI. Defining, establishing, and verifying reference intervals in the clinical laboratory; approved guideline—third edition. CLSI document C28-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2008.