Calcif Tissue Int (2000) 67:220–224
DOI: 10.1007/s002230001133

Calcified Tissue International

Peripheral Bone Mass is Not Affected by Winter Vitamin D Deficiency in Children and Young Adults from Ushuaia

M. B. Oliveri,* A. Wittich, C. Mautalen,* A. Chaperon, A. Kizlansky**

Sección Osteopatías Médicas, Hospital de Clínicas, Universidad de Buenos Aires, Córdoba 2351 (1120) Buenos Aires, Argentina and Servicio Clínica Medica, Hospital Regional de Ushuaia, Buenos Aires, Argentina

Received: 7 June 1999 / Accepted: 22 March 2000

Abstract. Low vitamin D levels in elderly people are associated with reduced bone mass, secondary hyperparathyroidism, and increased fracture risk. Its effect on the growing skeleton is not well known. The aim of this study was to evaluate the possible influence of chronic winter vitamin D deficiency and higher winter parathyroid hormone (PTH) levels on bone mass in prepubertal children and young adults. The study was carried out in male and female Caucasian subjects. A total of 163 prepubertal children (X age ± 1 SD: 8.9 ± 0.7 years) and 234 young adults (22.9 ± 3.6 years) who had never received vitamin D supplementation were recruited from two areas in Argentina: (1)Ushuaia (55° South latitude), where the population is known to have low winter 25OHD levels and higher levels of PTH in winter than in summer, and (2)Buenos Aires (34°S), where ultraviolet (UV) radiation and vitamin D nutritional status in the population are adequate all year round. Bone mineral content (BMC) and bone mineral density (BMD) of the ultradistal and distal radius were measured in the young adults. Only distal radius measurements were taken in the children. Similar results were obtained in age-sex matched groups from both areas. The only results showing significant difference corresponded to comparison among the Ushuaian women: those whose calcium (Ca) intake was below 800 mg/day presented lower BMD and BMC values than those whose Ca intake was above that level (0.469 ± 0.046 versus 0.498 ± 0.041 g/cm^2, $P < 0.02$; 3.131 ± 0.367 versus 3.339 ± 0.386 g, $P < 0.05$, respectively). In conclusion, peripheral BMD and BMC were similar in children and young adults from Ushuaia and Buenos Aires in spite of the previously documented difference between both areas regarding UV radiation and winter vitamin D status. BMD of axial skeletal areas as well the concomitant effect of a low Ca diet and vitamin D deficiency on the growing skeleton should be studied further.

Key words: Peripheral bone mass — Childhood bone mass — Peak bone mass — Vitamin D deficiency.

Low vitamin D levels in adults and elderly people are associated with reduced bone mass [1–3], secondary hyperparathyroidism, and increased fracture risk, all of which can be prevented by vitamin D supplementation [4, 5].

Previous studies carried out in Ushuaia (55°S), the southernmost city in Argentina, showed that approximately 50% of the children had low winter levels of 25 hydroxyvitamin D (25OHD) (below 8 ng/ml) [6, 7], which were normal at the end of the summer. These children also had higher PTH levels in winter than in summer [7]. A similar finding was reported in children living in Santander, Spain [8]. Lower serum winter levels of 25OHD in young women living in Ushuaia compared with the Buenos Aires age-matched population have also been reported [9].

Peak bone mass (PBM) is an important determinant of osteoporotic fracture risk [10]. PBM, which is mostly genetically determined, may be influenced by nutritional factors such as Ca and protein intake, physical activity [11, 12], and endocrine factors [10]. However, the influence of vitamin D status during growth on the attainment of PBM has been investigated scantily [13–15]. The objective of this study was to evaluate the possible influence of chronic winter vitamin D deficiency and higher winter parathyroid hormone (PTH) levels on the bone mass of prepubertal children and young adults. For this purpose, a group of children and young adults living in Ushuaia were compared with age- and sex-matched controls from Buenos Aires where UV radiation and vitamin D nutritional status in the population are adequate all year round. It is important to point out that the subjects included in the study had never received vitamin D supplementation.

Materials and Methods

Subjects

Caucasian Argentinian subjects were recruited as follows:

In Buenos Aires: Parents of 8 to 10-year-old primary school children were informed about the study and 180 agreed to have their children participate; 82 children were selected using a table of random numbers. Three were excluded because of previous vitamin D supplementation. Two hundred and fifty university students were informed about the study and 240 agreed to participate; of these, 122 were selected by a table of random numbers. Nobody was excluded.

In Ushuaia: Two hundred parents of school children were similarly informed; 182 agreed to have their children participate; of these, 110 were selected by a table of random numbers. Twenty-one were excluded because of previous vitamin D supplementation. Adults aged 18–30 years were invited to participate through television and radio announcements: 230 adults registered for the study, 120 of whom were selected by a table of random numbers. Eight subjects were excluded because of previous vitamin D supplementation. The total population included 168 prepubertal

Correspondence to: M. B. Oliveri, Sección Osteopatías Médicas Hospital de Clínicas, Cordoba 2351 (1120), Buenos Aires, Argentina

* Established investigator of CONICET (National Research Council Argentina)
** Fellow of CONICET

Table 1. Anthropometric data of the prepubertal children from Ushuaia and Buenos Aires (X ± SD)

	Girls		Boys	
	Ushuaia n = 51	Buenos Aires n = 40	Ushuaia n = 38	Buenos Aires n = 39
Age (years)	8.7 ± 0.7	9.1 ± 0.7	8.8 ± 0.7	9.2 ± 0.6
Height (cm)	129.2 ± 8.1	130.9 ± 7.7	130.6 ± 6.3	132.9 ± 5.3
Weight (kg)	30.2 ± 6.6	29.0 ± 6.7	30.4 ± 4.8	30.6 ± 4.5
Calcium intake (mg/day)	798 ± 303	816 ± 330	666 ± 268[a]	966 ± 344
Physical activity (hours/week)	8.5 ± 6.7	7.9 ± 3.0	10.3 ± 5.7	8.5 ± 4.0

[a] $P < 0.001$

children (ages 8–10 years) X ± SD: 8.9 ± 0.7 years and 234 young adults (ages 18–30 years), 22.9 ± 3.6 years of both sexes from both cities.

In Buenos Aires (34°S), a city in the central area of Argentina, previous reports have demonstrated adequate nutritional vitamin D status in the population [6, 7, 9] and adequate UV radiation for vitamin D photoproduction in the area [16]. In Ushuaia (55°S), the southernmost city in the world, there is a high incidence of low winter 250HD levels [6, 7, 9] and UV radiation and vitamin D photoproduction *in vitro* during the autumn and winter months is scant [16].

The subjects were physically healthy and were permanent residents of both areas since birth; none had ever received vitamin D supplementation prior to the study. The following exclusion criteria were applied: a previous history of renal, bone, or hepatic diseases; and weight or height below the 3rd or above the 97th percentiles, using charts for the normal Argentine population.

Methods

Informed consent was obtained from the children's parents and from the young adults prior to the measurements. Personal data were obtained in an interview. Height, weight, and body mass index (BMI) were measured; weight/height 2 was derived from those measurements.

A nutritional questionnaire, performed by the same registered dietician in both cities [17], evaluated weekly food and dairy products consumption. Total calorie, protein, and Ca intake were evaluated in the young adults. In the group of younger children, parents were asked to complete the nutritional questionnaire. Only Ca intake from dairy products was evaluated since we considered it more specific and more reliable than evaluating all the foods. In order to ensure that the participants had never received vitamin D supplementation, a list of the medications containing vitamin D (alone or in multivitamins) and of foods enriched with vitamin D was specifically mentioned during the interviews. Only a few foods (some low fat dairy products and types of cereal) are enriched with vitamin D in our country.

A physical activity questionnaire recording the time spent each week on the most common activities was completed by all the subjects (adapted from Slemenda et al.) [11].

Bone Mass Measurements. BMD and BMC of the distal and ultradistal nondominant arm were measured in the young adults by single energy X-ray absorptiometry (DXA) using a densitometer Osteometer DTX 100. The same DXA instrument was used in both cities. Only the distal radius was measured in the prepubertal children since the ultradistal radius was difficult to assess in the younger children.

Quality control was monitored daily during the study using a radius phantom provided by the manufacturer (Osteometer). The coefficient of variation in our laboratory was 0.85% and 0.99% for BMC and BMD measurements, respectively.

Statistics. Results are expressed as the mean ± 1 SD. Significance of difference was evaluated by a two-tailed Student's unpaired *t*-test. Multiple regression was applied to evaluate the influence of the different variables. The Statt View 512 software for Apple Macintosh was used.

Results

Anthropometric Data

Anthropometric data of the children are reported in Table 1. There were no differences in age, weight, or height between both populations. Anthropometric data of the young adults are shown in Table 2. There were no differences in age or weight between populations, but both males and females from Buenos Aires were taller than their corresponding Ushuaian group. Women from Buenos Aires had a lower BMI than women from Ushuaia (21.4 ± 2.0 versus 22.7 ± 2.4) ($P < 0.007$). There was no difference in BMI between the groups of men.

Bone Mass Measurements

Boys and girls from both cities had similar distal radius BMC, area, and BMD values (Table 3). Male and female young adults from both areas showed similar distal and ultradistal radius BMC, area, and BMD values (Table 4). The subjects in each group were regrouped according to age and their bone mass was compared (e.g., 18-year-olds, 19-year olds, etc. to 30-year-olds); there was no statistically significant difference within groups. Therefore, the whole group could be used to compare the population of both cities. Multiple regression analysis revealed no correlation between anthropometric, nutritional, or physical activity and the bone measurements. The only results showing significant difference corresponded to comparison among the Ushuaian women: those whose Ca intake was below 800 mg/day (n = 34) presented lower distal radius BMD and BMC values than those whose Ca intake was above that level (n = 31) (0.469 ± 0.046 versus 0.498 ± 0.041 g/cm^2 $P < 0.02$; 3.131 ± 0.367 versus 3.339 ± 0.386 g, $P < 0.05$, respectively).

No difference was found in any bone measurement

Table 2. Physical characteristics, nutritional evaluation, and physical activity in young adult women and men from Ushuaia and Buenos Aires (X ± 1 SD)

	Women		Men	
	Ushuaia n = 65	Buenos Aires n = 68	Ushuaia n = 47	Buenos Aires n = 54
Age (years)	22.8 ± 3.6	23.1 ± 3.6	21.9 ± 3.7	23.1 ± 3.2
Height (cm)	157.0 ± 6.0[b]	162.0 ± 6.1	170.1 ± 6.3[a]	173.6 ± 6.0
Weight (kg)	56.1 ± 7.1	55.9 ± 6.6	68.8 ± 11.3	71.0 ± 7.8
Energy (Kcal/day)	2333 ± 811[b]	1988 ± 665	3287 ± 876	2994 ± 995
Protein intake (mg/day)	102 ± 34	97 ± 30	135 ± 32	148 ± 5.5
Calcium intake (mg/day)	928 ± 656	971 ± 359	932 ± 610	1151 ± 625
Physical activity (hours/week)	7.1 ± 6.8	7.2 ± 4.7	7.4 ± 6.4	8.2 ± 4.7

[a] $P < 0.05$; [b] $P < 0.02$

Table 3. Bone measurements of prepubertal children

	Girls		Boys	
	Ushuaia	Buenos Aires	Ushuaia	Buenos Aires
Distal radius				
BMC (g)	1.631 ± 0.270	1.590 ± 0.212	1.843 ± 0.211	1.765 ± 0.186
Area (cm2)	5.160 ± 0.520	5.040 ± 0.460	5.410 ± 0.390	5.340 ± 0.340
BMD (g/cm2)	0.317 ± 0.039	0.318 ± 0.033	0.341 ± 0.026	0.330 ± 0.029

Table 4. Young adults bone mass measurements

	Girls		Boys	
	Ushuaia	Buenos Aires	Ushuaia	Buenos Aires
Distal radius				
BMC (g)	3.191 ± 0.373	3.120 ± 0.356	4.441 ± 0.458	4.226 ± 0.537
Area (cm2)	6.646 ± 0.447	6.563 ± 0.450	7.708 ± 0.519	7.531 ± 0.581
BMD (g/cm2)	0.481 ± 0.045	0.477 ± 0.039	0.575 ± 0.043	0.559 ± 0.047
Ultradistal radius				
BMC (g)	1.730 ± 0.41	1.770 ± 0.36	2.586 ± 0.499	2.646 ± 0.659
Area (cm2)	4.490 ± 0.738	4.450 ± 0.804	5.010 ± 0.722	5.263 ± 1.136
BMD (g/cm2)	0.395 ± 0.046	0.396 ± 0.050	0.518 ± 0.052	0.504 ± 0.061

among women from Buenos Aires or among men, girls, and boys from the two cities, when analyzed according to their Ca intake.

Nutritional and Physical Activity Questionnaire

The results of the nutritional and physical activity questionnaires are shown in Tables 1 and 2. Calorie intake of the young adult Ushuaian population was approximately 300 calories higher than the corresponding group from Buenos Aires, a difference that reached significance in the women ($P < 0.02$). Average Ca intake was found to be similar in all age- and sex-matched groups, except for the boys from Ushuaia whose Ca intake was significantly lower than their Buenos Aires controls ($P < 0.001$). Physical activity was similar in both areas—more than 90% of it was weight-bearing sports (running, walking, gym, soccer, and hockey). The groups of adults and children spent a similar amount of weekly hours on physical activity.

Discussion

Vitamin D deficiency has been shown to contribute to bone loss in elderly populations, presumably associated with secondary hyperparathyroidism [1]. In infants and children, marked vitamin D deficiency causes rickets, poor mineralization, bone deformities, and slow growth [18, 19]. Although severe osteopenia is associated with rickets, this measurement is not commonly used as a marker of treatment efficiency, nor is assessment of BMC commonly used in the follow-up of children with rickets. We have been unable to find information in the literature on the long-term consequence of transient osteopenia induced by vitamin D deficiency during childhood and adolescence.

We investigated whether living in Ushuaia–an area characterized by winter vitamin D deficiency and higher PTH levels—during childhood, adolescence, and youth might affect peripheral bone mass in children and attainment of peak bone mass in young adults. Age-matched groups from Buenos Aires were used as controls, since previous studies carried out by our laboratory showed this population to have an adequate vitamin D status and UV radiation all year round [6, 16, 20].

The results of the present study reveal that children and young adults living in Ushuaia since birth, and therefore suffering a winter vitamin D deficiency during growth [6, 7, 9], and who had not received vitamin D supplementation, had peripheral bone mass values similar to their age-matched controls from Buenos Aires.

Why did the winter vitamin D deficiency not affect bone mass during growth in the Ushuaian population? A possible explanation could be that the adequate 25OHD summer levels [7] might have compensated for the effect of the winter vitamin D deficiency and higher PTH levels on bone mass.

Recent studies carried out in France of young healthy women between 11 and 24 years of age showed a weak correlation between 25OHD levels and lumbar spine BMD, concluding that vitamin D might play a modest role in lumbar bone mineral acquisition during puberty [15]. Due to technical restraints, we only measured a peripheral non-weight-bearing area; we were not able to measure other axial skeletal areas that could be more sensitive to a vitamin D deficit. Future studies should evaluate the possible deleterious effect of vitamin D deficiency on the axial skeleton.

The different response of the elderly, who do suffer bone loss due to vitamin D deficiency and secondary hyperparathyroidism, could be explained by the fact that this age group has a lower intestinal Ca absorption capacity as well as a certain degree of resistance to the action of vitamin D [21–23]. Thus, they would easily and rapidly suffer a decrease in their Ca supply and a varying degree of secondary hyperparathyroidism, which would in turn cause a direct increase of bone resorption [1, 24], thus diminishing bone mass.

Calcium intestinal absorption is adequate in children, and even when 25OHD levels dropped, the slight increase of PTH during winter would maintain $1,25(OH)_2D$ levels which, together with the usual dietary Ca intake of our study population, would ensure adequate availability of this mineral for the skeleton. The only significant difference found in this study was within the female Ushuaian population: Ushuaian women whose Ca intake was below 800 mg/day had significantly lower BMD and BMC distal radius as compared with those whose Ca intake was above 800 mg/day. This difference might stress the importance of Ca intake for vitamin D-deficient populations.

Recent studies carried out in Reykjavik (64°N), Iceland [14] on young women between 16 and 18 years of age showed that there was no correlation between BMD values for total body, lumbar spine, hip, and forearm, and winter 25OHD levels. The only difference found was that the adolescents with lower 25OHD levels and lower Ca intake had the lowest bone mass values [14]. These results reinforce the importance of the interrelation between Ca intake and 25OHD levels, and the fact that adequate Ca intake can compensate for a vitamin D deficit. During growth, and especially during puberty, others factors such as the increase of sexual steroid hormones and of IGF 1 levels [10] might be more important for the attainment of peak bone mass than a seasonal vitamin D deficit.

Krabbe et al. [25] showed the existence of a relation between sexual steroid hormones and bone mass, yet they could not establish a clear relation between vitamin D metabolites and bone mass. It must be pointed out that whereas these authors studied a group of pubertal males with above normal 25OHD levels, the Ushuaian population included in this study presumably had low 25OHD levels all their life.

Another factor that might have protected the bone mass of the Ushuaian children and young adults is their adequate physical activity—mainly weight-bearing activities, which, according to several studies reported in the literature, have the greatest positive effect on bone mass [11, 12, 26, 27].

A surprising finding was that the height of both Ushuaian young males and females was significantly lower than their age-matched controls. Calorie and protein intake were similar in both groups, although it must be pointed out that the questionnaire assessed intake only at the time of the study, not throughout their life span. The influence of vitamin D status on growth cannot be totally discarded. Studies comparing length of the body trunk and legs would contribute to determining whether this difference is accounted for by a lesser growth of the legs. A larger population must be studied in order to eliminate any bias arising from the limited number of subjects.

Our results show evidence that there are no differences between the Buenos Aires population and their age-and sex-matched controls from Ushuaia regarding BMD and BMC of the distal radius (children) and BMD and BMC of the distal and ultradistal radius (young adults). However, further studies to determine whether the axial skeletal areas are affected by winter vitamin D deficiency and higher PTH levels during growth would be useful in order to confirm whether the difference in vitamin D levels affects any segment of the growing skeleton.

Acknowledgments. This study was supported in part by the National Council of Research (Conicet), by the Fundación Argentina de Osteología, and by Nestlé Argentina S.A.

References

1. Khaw KT, Sheyd MJ, Compston J (1992) Bone density, parathyroid hormone and 25 hydroxyvitamin D concentrations in middle-aged women. Br Med J 305:273–277
2. Villareal DT, Civitelli R, Chines A, Avioli LV (1991) Subclinical vitamin D deficiency in postmenopausal women with low vertebral mass. J Clin Endocrinol Metab 72:628–634
3. Ooms ME, Lips P, Roos JC, van der Vijghw JF, Popp-Smijders C, Bezemer PD, Bouter LM (1995) Vitamin D status and sex hormone binding globulin: determinants of bone turnover and bone mineral density in elderly women. J Bone Miner Res 10:1177–1184
4. Chapuy MC, Arlot ME, Delmas PD, Meunier PJ (1994) Effect of calcium and cholecalciferol treatment for three years on hip fractures in elderly women. Br Med J 308:1081–1082
5. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE, Falconer G, Green CL (1995) Rates of bone loss in postmenopausal women randomly assigned to one of two dosages of vitamin D. Am J Clin Nutr 61:1140–1145
6. Oliveri MA, Ladizesky M, Sotelo A, Griffo S, Ballesteros G, Mautalen C (1991) Nutritional rickets in Argentina. In: Glorieux F (ed) Rickets. Raven Press, Nestlé Nutrition Workshop Series, Vol 21, pp 233–245

7. Oliveri MB, Ladizesky M, Mautalen CA, Alonso A, Martinez L (1993) Seasonal variations of 25 hydroxyvitamin D and parathyroid hormone in Ushuaia (Argentina). The southernmost city of the world. Bone Miner 20:99–108
8. Docio S, Riancho JA, Pérez A, Olmos JM, Amado JA, González Macías J (1998) Seasonal deficiency of vitamin D in children: a potential target for osteoporosis-preventing strategies? J Bone Miner Res 13:544–548
9. Oliveri MB, Mautalen CA, Alonso A, Velazquez H, Trouchot HA, Porto R, Martinez L, Barata AD (1993) Estado nutricional de vitamina D en madres y neonatos de Ushuaia y Buenos Aires.Medicina (Buenos Aires) 53:315–320
10. Bonjour JP, Theintz G, Law F, Slosman D, Rizzoli R (1994) Peak bone mass. Osteoporosis Int (suppl)1:S7–S13
11. Slemenda ChW, Miller JZ, Hui SL, Reister TK, Johnston CC (1991) Role of physical activity in the development of skeletal mass in children. J Bone Miner Res 6:1227–1233
12. Courteix D, Lespessailles E, Loiseau Peres S, Obert P, Germain P, Benhamou CL (1998) Effect of physical training on bone mineral density in prepubertal girls: a comparative study between impact-loading and nonimpact-loading sports. Osteoporosis Int 8:152–158
13. Fehily AM, Coles RJ, Evans WD, Elwood PC (1992) Factors affecting bone density in young adults. Am J Clin Nutr 56: 579–586
14. Sigurdsson G, Kristinsson JB, Valdi Marssun O, Franzson L, Steimgrimsdottir L (1997) How important is vitamin D for normal bone mineralization in adolescent girls? 3rd Interl Symp on Nutritional Aspects of Osteoporosis, p13. Laussane, Switzerland, May 1997
15. Marcelli C, Souquières G, Sabatier JP, Walrant O, Garabedian M (1998) Vitamin D and bone mineral acquisition in females during adolescence. Osteoporosis Int 8:S3–S42
16. Ladizesky M, Lu Z, Oliveri B, San Roman N, Diaz S, Holich M, Mautalen C (1995) Solar ultraviolet B radiation and photoproduction of vitamin D3 in central and southern areas of Argentina. J Bone Miner Res 10:545–549
17. Rovirosa A, Dupraz H, de Portela MLPM, Río ME (1993) Ingesta de nutrientes en una población estudiantil masculina de la Universidad de Buenos Aires. Rev Farm 135:53–61
18. David L (1991) Common vitamin D deficiency rickets. In: Glorieux F (ed) Rickets. Raven Press, Nestlé Nutrition Workshop, series vol 21, pp 107–122
19. Brooke OG, Butters F, Wood C (1991) Intrauterine vitamin D nutrition and postnatal growth in Asian infants. Br Med J 41:205–214
20. Ladizesky M, Oliveri B, Mautalen CA (1987) Niveles séricos de 25-hydroxi-vitamin D en la población normal de Buenos Aires: su variación estacional. Medicina (Buenos Aires) 47: 268–272
21. Francis RM, Peacock M, Storer JH, Davies AEJ, Brown WB, Nordin BEC (1983) Calcium malabsorption in the elderly: the effects of treatment with oral 25 hydroxyvitamin D3.Eur J Clin Invest 13:391–396
22. Ebeling PE, Sandgren MC, Di Magno EP, Lane AW, De Luca H, Riggs L (1992) Evidence of an age-related decrease in intestinal responsiveness to vitamin D: relationship between serum 1-25 dihydroxyvitamin D3 and intestinal vitamin D receptor concentrations in normal women. J Clin Endocrinol Metab 75:176
23. Gallagher JC, Riggs BL, Eisman J et al. (1979) Intestinal calcium absorption and serum vitamin D metabolites in normal subjects and osteoporotic patients. J Clin Invest 64:729–736
24. Kamel S, Brazier M, Picard C, Bortte F, Sanson L, Desmet G, Sebert JL (1994) Urinary excretion of pyridinoline crosslinks measured by immunoassay and HPLC techniques in normal subjects and in elderly patients with vitamin D deficiency. Bone Miner 26:197–208
25. Krabbe S, Christiansen C, Hummer L (1986) Serum vitamin D metabolites are not related to growth rate, bone mineral content or serum alkaline phosphatase in male puberty. Calcif Tissue Int 38:127–129
26. Morris FL, Naughton GA, Gibbs JL, Carlson JS, Wark JP (1997) Prospective ten-month exercise intervention in premenarchal girls: positive effects on bone and lean mass. J Bone Miner Res 12:1453–1462
27. Specker B (1996) Evidence for interaction between calcium intake and physical activity on changes in bone mineral density. J Bone Miner Res 11:1539–1544