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Positive association between the course of vitamin D intake and bone mineral density at 36 years in men

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ABSTRACT

Introduction: Studies on the association of vitamin D and bone mineral density (BMD) in adolescence and young adults have shown contrasting results. None of these studies have examined the course and baseline in vitamin D intake. The purpose of this study was to examine the association between baseline and the course of dietary vitamin D intake on the BMD.

Methods: Vitamin D intake was assessed 3–8 times between the age of 13 and 36 years in 152 men and 168 women from the Amsterdam Growth and Health Longitudinal Study. The BMD of the femoral neck, lumbar spine, total hip and total body was measured at the age of 36 years with dual-energy X-ray absorptiometry. Linear regression analyses were used to determine the vitamin D intake pattern in time for each subject. The models provide a baseline, course and fluctuation of the vitamin D intake for each subject. These were used in separate regression analyses with the dependent variable BMD.

Results: Mean baseline vitamin D was 6.86 (SD: 2.18) µg/day for men and 4.90 (1.19) µg/day for women. Mean course of vitamin D was –0.10 (0.12) µg/day/year and –0.05 (0.18) µg/day/year for men and women respectively. After adjustment for potential confounders and correcting for the other parameters of vitamin D intake, the associations between baseline vitamin D intake and BMD were significant in the total hip (0.018 g/cm² per –1 µg/day;

95% CI 0.001–0.035) and total body (0.015 per – 1 µg/day; 0.001–0.029). The course of vitamin D intake was associated with BMD in the lumbar spine (0.50 g/cm² per – 1 µg/day/year; 0.130–0.867), femoral neck (0.42 g/cm² per – 1 µg/day/year; 0.10–0.743), total body (0.34 g/cm² per – 1 µg/day/year; 0.09–0.59) and total hip (0.44 g/cm² per – 1 µg/day/year; 0.11–0.77) in men. No significant associations were found in women.

Conclusion: In men, the level of vitamin D intake in adolescence and the course of vitamin D intake from adolescence into adulthood are positively related with BMD in adulthood. In women, however, no significant associations are found.

INTRODUCTION

Worldwide, osteoporosis is an important cause of morbidity, mortality and medical costs [1]. It affects millions of people and the prevalence is increasing [2]. One of the characteristics of osteoporosis is low bone mineral density (BMD) [3]. BMD is influenced by genetic and environmental factors like physical activity, the amount of sunlight, and dietary factors including calcium, potassium, fiber, and vitamin D [4], [5], [6] and [7]. Serum 25-hydroxyvitamin D was found to have a positive association with BMD [7], [8], [9] and [10]. The main source of vitamin D is the cutaneous production through sunlight, which is influenced by the time of day, season and latitude. The dietary intake of vitamin D, however, also plays a role in the development and maintenance of an adequate BMD [11], [12], [13], [14] and [15].

The active vitamin D metabolite 1,25-dihydroxyvitamin D has a major role in maintaining serum calcium concentrations within the physiologically acceptable range [16]. Therefore, vitamin D deficiency results in abnormalities in calcium metabolism and can lead to a decrease in bone mineralization [16]. Vitamin D works in three ways; 1,25-dihydroxyvitamin D suppresses the parathyroid hormone, which stimulates bone resorption [17], 1,25-dihydroxyvitamin D stimulates the absorption of calcium from the intestine [18] and 1,25-dihydroxyvitamin D leads to reduced RANKL expression and delayed osteoclastogenesis with as a consequence transient increase in bone volume [19].

Studies on vitamin D and BMD mainly have been focussed on elderly, postmenopausal women and young children. In adolescence and young adults, some studies report a positive association [17], [20], [21] and [22], whereas others report no association between vitamin D and BMD [23], [24], [25] and [26]. The two studies that adjusted their analyses for potential confounders showed positive associations [17] and [22]. To our knowledge, there have been no prospective studies that have examined the relationship between vitamin D intake through diet and BMD. Therefore, we examined the role of different aspects of long-term vitamin D intake through diet from 13 to 36 years of age on bone mineral density at the age of 36 years.

MATERIALS AND METHODS

Study design

The Amsterdam Growth and Health Longitudinal Study (AGAHLS) is a longitudinal observational study that started in 1977. It started with a group of girls and boys of 13 years of age from two secondary schools in the Netherlands. The AGAHLS was planned to monitor the growth, health and lifestyle of boys and girls over a period of 4 years. The study was extended with measurements at the age of 21, 27, 29, 32 and 36 years. At each follow-up, health factors, psychological factors and lifestyle factors were assessed. The study was approved by the medical ethics committee of the VU University Medical Center and all

subjects gave their written informed consent (provided by the parents when subjects were aged 13–16 years) at each follow-up.

Subjects

At the age of 13 years 698 individuals were included. In 2000 at the age of 36 years 380 individuals were still in the study. To be included in the analyses for this paper, the following criteria were used: 1) Caucasian ethnicity, because skin colour is important for the vitamin D synthesis through sunlight [27]. 2) Dietary vitamin D data were available from at least 3 follow-up measurements and 3) BMD data were available at the follow-up at the age of 36 years.

Measurements

Bone mineral density

Bone mineral density at the age of 36 years was measured at the lumbar spine (L1–L4), femoral neck, total hip, and in the total body with dual-energy X-ray absorptiometry (DXA) using the Hologic QDR-2000 (S/N 2513; Hologic, Inc., Waltham, MA, USA) in the period March–June 2000. For the lumbar spine, BMD of each lumbar vertebral body was measured and the average of the L1–L4 was used in the analysis.

Vitamin D intake

The vitamin D intake through diet was assessed at the ages 13, 14, 15, 16, 21, 27, 32 and 36 years. At the first seven measurements dietary intake was assessed through detailed cross-check dietary history interview based on the method developed by Beal [28] and Marr [29]. The interview provided information about the usual dietary intake within a reference period of 4 weeks. The method consisted of 2 parts. In the first part the individual was instructed to describe the meals on a typical work/school day and on a weekend day. The second part was a check on the first part. It consisted of a structured interview with the use of a checklist. All the consumed foods were checked for the last 4 weeks. Only foods that were consumed at least twice a month were taken into account. The amount of consumed food was assessed with the aid of models of for example glasses, spoons and sizes of potatoes and fruit. During adolescence, the parents of the subjects were asked to provide additional information about the preparation and details of the consumed meal, because they were assumed to know this better than the teenagers.

At the last measurement at the age of 36 years, the dietary intake was assessed through an interviewer-administered computer-assisted version of the cross-check dietary history interview. The same interview, structure, reference period, questions and database were used. Agreement between the two methods was sufficiently high (Cohen's kappa ranged from 0.4 to 0.8) [30]. For each individual the amounts of consumed food were expressed in grams per week. The Dutch food table of 2004 was used to convert the information about food into μg of vitamin D per day [31]. Main sources of vitamin D are fatty fish (salmon, mackerel) and margarine.

Covariates

Calcium intake

Calcium intake was assessed in the same way as vitamin D

Occupation

Three occupational groups were formed with regard to sunlight exposure. Group 1 is outdoor work (gardener, cycle courier, market trader etc.); group 2 is indoor work (work at office, nurse, teacher etc.) and group 3 is partly outdoor/partly indoor (stewardess, postman etc.).

Weight bearing physical activity (MECHPA)

Weight bearing physical activity is expressed as the amount of biomechanical ground reaction forces (GRF). From 13 to 32 years of age habitual physical activities (PA) were assessed using a structured interview with a reference period of 3 months [32]. At the age of 36 years an identical interviewer-administered computer-assisted version of the PA interview was used. Activities were categorised and given a score from 0 for activities such as swimming and cycling etc., up to a score 3 for activities with the highest GRF, such as basketball, indoor soccer, and volleyball. The sum of all the GRF's, irrespective of the duration, intensity and frequency of the activity, is the MECHPA score.

Metabolic physical activity (METPA)

Metabolic physical activity was assessed in the same way as weight-bearing physical activity. Only physical activities with a non-stop duration of 5 min and an intensity of at least four times the resting metabolic rate (RMR) were taken into account. The activities were categorized into three groups: light ($4-7 \times \text{RMR}$), medium ($7-10 \times \text{RMR}$) and heavy ($> 10 \times \text{RMR}$). Average RMR (5.5, 8.5 and 11.5) values were used to add up all the activities. The METPA is the RMR times the duration of the activities performed.

Body weight

Subjects, dressed only in underwear, had their body weight measured to the nearest 0.1 kg on a spring balance scale (van Vucht, Amsterdam, The Netherlands).

Statistical analysis

Drop-out analyses were performed based on the mean of the first 4 years of measurement (13–16 years of age). Drop-outs were defined as subject for whom no data were obtained at the age of 36 years of age. Independent *T*-tests were performed for men and women separately to compare drop-outs with non-drop-outs on vitamin D intake and all the putative confounders, with the exception of occupation, for which a χ^2 test was performed.

Linear regression analyses were used to model the vitamin D intake for each subject from 13 to 36 years of age. The intercept of the individual regression line denotes the estimated baseline vitamin D intake at the age of 13 years, The regression coefficient for time denotes the mean (linear) course of vitamin D intake over the period of follow-up (in μg vitamin D per day during the year) and the standard error of the estimate provides an indication of the fluctuation of the course over time.

[TABLE 1]

The baseline and course of vitamin D intake of all subjects were put into separate regression models for each BMD measurement (lumbar spine, femoral neck, total hip, and total body). Subsequently, the parameters were mutually adjusted, and were adjusted for the fluctuations in vitamin D intake. Finally, the corrected models were further adjusted for occupation, body weight, METPA, MECHPA, and calcium intake. Separate analyses were performed for males and females. Analyses were performed using SPSS 14.0.

RESULTS

Loss to follow-up

At baseline, at the age of 13 years, the study group consisted of 331 men and 367 women of whom 174 men and 187 women had complete data at the last measurement at the age of 36 years. 152 (87%) men and 168 (90%) women were included in the analyses after exclusion of participants with a non-Caucasian background and of participants who had attended less than 3 measurement waves. The drop-out analysis showed that both male and

female participants and non-participants did not differ significantly on vitamin D intake or on any of the covariates.

Baseline characteristics

The characteristics of the study group are presented in Table 1. The average baseline vitamin D intake was 6.86 (SD 2.18) $\mu\text{g/day}$ for men and 4.90 (1.19) $\mu\text{g/day}$ for women. Vitamin D intake decreased from 13 to 36 years of age with an average of 0.10 (0.12) and 0.05 (0.18) $\mu\text{g/day}$ per year in men and women, respectively, what was mainly caused by the decreases in margarine and milk intake. At the age of 36 years, around 94% of the participants had an indoor job.

Relationship between vitamin D intake and BMD

Table 2 and Table 3 show the results of the regression analyses for men and women respectively.

[TABLE 2]

[TABLE 3]

In men, significant positive associations were found for baseline vitamin D intake and BMD in all categories in the corrected model, ranging from 0.017 g/cm^2 (95% CI 0.005–0.030) for total body to 0.020 g/cm^2 for the other categories of BMD. However, after adjusting for calcium intake, occupation, MECHPA, METPA and weight, only the relationship with total hip and total body remained significant. The results of the analyses indicate that for two subjects with the same slope over time and an average difference of 1 $\mu\text{g/day}$ vitamin D intake over a period of 25 years, a difference in BMD of the total hip of 0.018 g/cm^2 (95% CI 0.001–0.035) and for the total body of 0.015 g/cm^2 (95% CI 0.001–0.029) will be found.

For the course of vitamin D intake, the corrected and adjusted models showed a highly significant positive association with all categories of BMD in men (see Table 2). The magnitude of the regression coefficients indicate that when a subject who does not change vitamin D intake over time is compared to a subject with an average decrease in vitamin D intake of 0.1 $\mu\text{g/day}$ over a period of 25 years, BMD will differ with 0.034 g/cm^2 (95% CI: 0.009–0.059) for the total body and with 0.050 g/cm^2 (95% CI: 0.013–0.087) for the lumbar spine after correcting for the other aspects of vitamin D intake and for potential confounders.

Women showed near to zero non-significant associations between the two indicators of vitamin D intake and all BMD measures in all analyses (see Table 3). All the coefficients were close to zero.

DISCUSSION

To our knowledge this is the first study that has examined the development of vitamin D intake through diet during adolescence and young adulthood in association with BMD at young adult age. Overall, the results of this study show that an increase in vitamin D intake from adolescence into adulthood is associated with a higher BMD at the age of 36 years in men. The analyses also showed significant positive associations in men between baseline vitamin D intake and BMD that was assessed more than two decades later. In women, no significant associations were found between vitamin D intake and BMD.

In the present study a positive association was found between baseline vitamin D intake and BMD in men. It is difficult to compare our study to other studies on the association between vitamin D and BMD. First, other studies have examined the serum 25-hydroxyvitamin D concentration and not the vitamin D intake through diet [7], [8], [9] and [10]. The correlation between the vitamin D intake through diet and serum 25-hydroxyvitamin D has been shown to be significant but low ($r = 0.25$) [23]. Second, our study is longitudinal whereas previous

studies were cross-sectional. Finally, most of the studies were conducted in Scandinavian countries or in populations with a different age distribution. The study with which our study can be best compared to is that of Bisschoff-Ferrari et al. [21], which found a positive association between 25-hydroxyvitamin D and BMD in white Americans at the age of 35 years.

The largest association of the course of vitamin D intake was found for BMD of the lumbar spine, the femoral neck and total hip. These sites are especially vulnerable for osteoporosis. Not all the bones are vulnerable to osteoporosis, which could explain the lower coefficient in the association of the course in vitamin D intake and BMD of the total body.

In women, no association between vitamin D and BMD was found. One reason for this could be that women's hormones like estrogen play an important role in the regulation of bone before the menopause. Estrogen's primary activity in bone is the inhibition of bone resorption [33]. However, other studies have found significant associations of 25-hydroxyvitamin D with BMD in women before the menopause [17] and [20]. Another reason could be that women tend to underreport their food intake [34], [35] and [36]. This could have influenced the association between the intake of vitamin D and BMD non-differential.

Clinical relevance

In the present study, a decrease in vitamin D intake of $-0.10 \mu\text{g/day}$ per year was associated with a 0.34 to 0.50 g/cm^2 lower BMD in men after 23 years. This corresponds with 0.33 standard deviation units in this group. In light of clinical relevance this seems of little importance because osteopenia is defined as a standard deviation between -1.0 and -2.5 and osteoporosis as a BMD below -2.5 standard deviations. However, one must realize that the population consist of young adults who have just attained their peak bone mass.

Limitations

This study has some methodological limitations. First, the most accurate measurement of vitamin D are blood levels of 25 (OH)D. Unfortunately, we did not have blood levels. In our analyses we tried to correct for the intake of vitamin D from sunlight by adjusting for occupation. Adjustment for occupation, however, did not influence the associations found between vitamin D and BMD. Second, some participants had attended only three measurement waves. This resulted in less reliable estimates from the individual regression analyses. Furthermore, we have assumed that the dietary tables were accurate. However, errors could have been made in the acquisition of the dietary intake through recall and misclassification bias and in the conversion from food intake to vitamin D intake. Because this was probably not differential, this would have led to an underestimation of the coefficients. In addition, the vitamin D level in fatty fish are variable and season dependent [37], which could have led to significant under or over estimation in vitamin D intake. Last, the average dietary vitamin D intake of our participants was nearly twice the recommended dietary allowance (RDA) in the Netherlands ($2.5 \mu\text{g/day}$). Only 2% of the men and 6% of the women had a baseline vitamin D intake below the recommended dietary allowance. Lower intakes may show different associations with BMD than those that were found here. However, the RDA is relatively low with regard to the publication of Bischoff-Ferrari et al. [38].

Conclusion

This study shows that the course of vitamin D intake from adolescence to young adulthood is positively associated with BMD in young male adults. Besides this, also vitamin D intake in adolescence is positively related with BMD in adulthood. For BMD of young female adults, the dietary vitamin D intake during adolescence and young adulthood does not seem to play a role.

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TABLES

Table 1

Characteristics of the male and female participants at the age of 36 years^a

Characteristics	Men (n = 152)	Women (n = 168)
Baseline Vit. D intake (µg/day)	6.86 (2.18)	4.90 (1.19)
Course of Vit. D intake (µg/day/year)	-0.10 (0.12)	-0.05 (0.18)
Fluctuations of Vit. D intake		
Median (IQR)	1.27 (0.81–1.80)	0.87(0.49–1.30)
BMD lumbar spine (g/cm ²)	1.09 (0.15)	1.07 (0.12)
BMD femoral neck (g/cm ²)	0.94 (0.13)	0.86 (0.12)
BMD total hip (g/cm ²)	1.07 (0.14)	0.96 (0.12)
BMD total body (g/cm ²)	1.20 (0.10)	1.09 (0.07)
Calcium intake (mg/day)	1425 (600)	1264 (410)
Occupation		
Outdoor	2.7%	1.4%
Indoor	94.6%	93%
MECHPA		
Median (IQR)	9 (7–12)	9 (6–11)
METPA (kMET*min*week ⁻¹)		
Median (IQR)	3.8 (2.2–5.8)	4.5 (2.9–6.8)
Body weight (kg)		
Median	80.6 (76.5–90.7)	66.5 (61.0–72.7)

^a Data presented indicate the mean and (SD).

Table 2

Linear regression coefficients with 95% confidence intervals (CI) of the baseline and course of vitamin D intake with BMD of the lumbar spine, femoral neck, total hip and total body for men

	Crude		Corrected ^a		Corrected ^a and adjusted ^b	
	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
Baseline						
Lumbar spine	-0.002	-0.014-0.010	0.020	0.001-0.038	0.017	-0.002-0.037
Femoral neck	0.000	-0.010-0.010	0.020	0.004-0.036	0.016	-0.001-0.033
Total hip	-0.001	-0.011-0.010	0.020	0.004-0.037	0.018	0.001-0.035
Total body	0.002	-0.006-0.010	0.017	0.005-0.030	0.015	0.001-0.029
Course						
Lumbar spine	0.286	0.082-0.490	0.530	0.184-0.877	0.498	0.130-0.867
Femoral neck	0.208	0.031-0.384	0.474	0.173-0.774	0.422	0.100-0.743
Total hip	0.217	0.035-0.399	0.502	0.192-0.811	0.440	0.113-0.767
Total body	0.150	0.013-0.286	0.372	0.143-0.602	0.339	0.087-0.591

^a Corrected for the other two parameters of vitamin D intake (either course and fluctuation, or baseline and fluctuation).

^b Adjusted for calcium intake, occupation, MECHPA, METPA and Weight.

Table 3

Linear regression coefficients with 95% confidence intervals (CI) of the baseline and course of vitamin D intake with BMD of the lumbar spine, femoral neck, total hip and total body for women

	Crude		Corrected ^a		Corrected ^a and adjusted ^b	
	Coefficient	95% CI	Coefficient	95% CI	Coefficient	95% CI
Baseline						
Lumbar spine	-0.003	-0.013-0.008	-0.006	-0.022-0.011	-0.003	-0.020-0.015
Femoral neck	-0.002	-0.012-0.008	-0.003	-0.019-0.013	-0.001	-0.018-0.016
Total hip	-0.002	-0.012-0.008	-0.005	-0.021-0.012	-0.003	-0.020-0.014
Total body	0.000	-0.006-0.007	-0.003	-0.013-0.008	-0.002	-0.013-0.009
Course						
Lumbar spine	-0.031	-0.143-0.080	-0.037	-0.373-0.299	0.022	-0.325-0.370
Femoral neck	-0.016	-0.126-0.094	0.009	-0.323-0.341	0.035	-0.305-0.372
Total hip	-0.032	-0.146-0.082	-0.026	-0.369-0.317	0.004	-0.344-0.351
Total body	-0.043	-0.115-0.029	-0.040	-0.255-0.175	-0.021	-0.239-0.198

^a Corrected for the other two parameters of vitamin D intake (either course and fluctuation, or baseline and fluctuation).

^b Adjusted for calcium intake, occupation, MEHPA, METPA and weight.