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Do sufficient vitamin D levels at the end of summer in children and adolescents provide an assurance of vitamin D sufficiency at the end of winter? A cohort study

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Abstract

Background: The changes in serum 25-hydroxyvitamin D (25(OH)D) in adolescents from summer to winter and optimal serum vitamin D levels in the summer to ensure adequate vitamin D levels at the end of winter are currently unknown. This study was conducted to address this knowledge gap.
Methods: The study was conducted as a cohort study. Sixty-eight participants aged 7–18 years and who had sufficient vitamin D levels at the end of the summer in 2011 were selected using stratified random sampling. Subsequently, the participants' vitamin D levels were measured at the end of the winter in 2012. A receiver operating characteristic (ROC) curve was used to determine optimal cutoff points for vitamin D at the end of the summer to predict sufficient vitamin D levels at the end of the winter.
Results: The results indicated that 89.7% of all the participants had a decrease in vitamin D levels from summer to winter: 14.7% of them were vitamin D-deficient, 36.8% had insufficient vitamin D concentrations and only 48.5% where able to maintain sufficient vitamin D. The optimal cutoff point to provide assurance of sufficient serum vitamin D at the end of the winter was 40 ng/mL at the end of the summer. Sex, age and vitamin D levels at the end of the summer were significant predictors of non-sufficient vitamin D at the end of the winter.
Conclusions: In this age group, a dramatic reduction in vitamin D was observed over the follow-up period. Sufficient vitamin D at the end of the summer did not guarantee vitamin D sufficiency at the end of the winter. We found 40 ng/mL as an optimal cutoff point.

Keywords: 25-hydroxyvitamin D; adolescents; children; vitamin D deficiency.

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Introduction

Vitamin D is a hormonal precursor with an essential role in mineral homeostasis and bone metabolism. Observed to play a role in major organs such as the brain and heart, it aids in prostate, colon and immune cell regulation [1–4], with deficiency being associated with various skeletal and non-skeletal diseases such as rickets [5], diabetes, hypertension [2, 3], cancer, cardiovascular and autoimmune diseases [6–8] and chronic illnesses. Vitamin D is also related to glycated hemoglobin (HbA_{1c}) levels [2] and postural sway [9]. Vitamin D is activated by adequate exposure to solar ultraviolet (UV)-B radiation or individual consumption of dietary supplements [10–13]. A common cause of vitamin D deficiency is, therefore, inadequate sun exposure [14–18]. Several studies have shown changes in seasons and geographical location can deeply affect levels in vitamin D serum [19–24]. In northern Iran, vitamin D deficiency in healthy school children and adolescents is particularly high [18], especially during the winter season [25].

The first phase of this study was conducted in 2011 in children whose ages ranged from 7 to 18 and who lived in Bojnourd (36° 21″ N). We noted a high prevalence of vitamin D deficiency and insufficiency in the children studied [18]. In this study, we investigated changes in serum vitamin D levels in children and adolescents (7–18 years) with sufficient vitamin D. We aimed to establish an optimal cutoff point for 25-hydroxyvitamin D (25(OH)D) in the summer to ensure adequate vitamin D levels at the end of the winter.

Materials and methods

Subjects

It was a prospective, observational, single-arm cohort study based on cross-sectional study samples from Habibesadat et al. [18] obtained in 2011 and 2012. Vitamin D levels of 361 healthy children aged 7–18 years were evaluated during the last 2 weeks of the summer in 2011 in northeastern Iran. Two hundred and twelve (58.7%) of these children had sufficient vitamin D levels (25(OH)D ≥30 ng/mL); 68 participants (52 boys and 16 girls) were selected using a stratified random sampling method. The 68 participants' vitamin D levels were measured again during the last 2 weeks of the winter in 2012.

Data collection

The parents of each participant were asked to fill a brief questionnaire in Persian. The questionnaire was given to them by their children, who were responsible for returning it to the researchers. Older participants completed the questionnaire by themselves. The questionnaire included questions such as duration of exposure to sunlight during the previous winter, travel to tropical areas, swimming in outdoor pools, clothing type and use of sunscreen (i.e. extent of body exposure). Sampling was performed at schools in the presence of a physician and two nurses.

25-Hydroxyvitamin D measurement

Serum 25(OH)D was measured using an enzyme immunoassay (EIA) kit (Roche Diagnostics GmbH, Mannheim, Germany). The IDS 25-hydroxyvitamin D EIA kit is an enzyme immunoassay for the quantitation of 25(OH)D and other hydroxylated metabolites in serum or plasma.

Statistical analysis

We used three categories for vitamin D status: vitamin D deficiency (25(OH)D <20 ng/mL), vitamin D insufficiency (20 ng/mL ≤25(OH)D <30 ng/mL) and vitamin D sufficiency (25(OH)D ≥30 ng/mL) [26]. A receiver operating characteristic (ROC) curve for vitamin D levels was then used to find the optimal cutoff points of vitamin D at the end of summer to discriminate between sufficient and non-sufficient (<30 ng/mL) vitamin D levels at the end of winter, according to the Youden index. Analysis was performed using the independent t-test, paired t-test and repeated measures analysis of variance (RMANOVA). A multiple log-binomial regression model was used to estimate relative risks (RRs) of predictors of non-sufficient vitamin D levels at the end of the winter. All statistical analyses were performed using Stata 14 for Windows. p-Values <0.05 were considered statistically significant.

Ethics statement

This study was approved by the Ethics Committee of North Khorasan University of Medical Sciences (the ethics permission code of this study is E5-1390-07-06).

Results

The mean age of the participants in this study was 12.9 ± 2.9 years. The difference in mean age for males and females was not significant (p = 0.085). The mean body mass index (BMI) of the study participants was 18.9 ± 3.8 kg/m^2. There was no significant difference between males and females (p = 0.863). The mean serum concentration of 25(OH)D in the study samples at the end of the summer were 46.5 ± 10.1 ng/mL (i.e. the study sample were vitamin D-sufficient). In 89.7% of the subjects studied, there was a decrease in vitamin D levels from the end of summer to the end of the winter. At the end of the winter, 14.7% of the children were vitamin D-deficient and 36.8% were vitamin D-insufficient (Table 1). There was a statistical difference in vitamin status in boys and girls and between the different age groups at the end of the winter.

The mean decrease in 25(OH)D was 15.3 ± 12.4 ng/mL (Table 2). The decrease in the concentrations of vitamin

Table 1: Vitamin D status of participants at the end of the winter by age and sex.

	Vitamin D at the end of winter			p-Value
	Non-sufficient			
	Deficient, n (%)	Insufficient, n (%)	Sufficient, n (%)	
All participants	10 (14.7)	25 (36.8)	33 (48.5)	
Sex				
Girls	6 (37.5)	6 (37.5)	4 (25.0)	0.008
Boys	4 (7.7)	19 (36.5)	29 (55.8)	
Age, years				
7–12	1 (3.1)	13 (40.6)	18 (56.3)	0.039
13–18	9 (25.0)	12 (33.3)	15 (41.7)	

All applicants were vitamin D-sufficient (25(OH)D ≥30 ng/mL) at the end of the summer.

Table 2: Mean ± SD vitamin D concentrations at each time point and its changes from the end of summer to the end of the winter.

	n	Stage 1: end of summer, ng/mL	Stage 2: end of winter, ng/mL	Changes, ng/mL	p-Value
Sex					
Girls	16	41.2 ± 8.2	23.9 ± 8.9	−17.3 ± 7.5	<0.001
Boys	52	48.1 ± 9.8	33.5 ± 12.8	−14.6 ± 13.6	<0.001
Age, years					
7–12	32	45.9 ± 9.7	34.7 ± 13.7	−11.2 ± 12.3	<0.001
13–18	36	46.9 ± 10.1	28.2 ± 10.6	−18.7 ± 11.5	<0.001
Total	68	46.5 ± 9.9	31.2 ± 12.6	−15.3 ± 12.4	<0.001

D from summer to winter were more pronounced in girls than in boys; however, this difference was not statistically significant, as determined by RMANOVA ($p = 0.453$). The mean concentrations of 25(OH)D were reduced from summer to winter, in both 7–12-year-olds and 13–18-year-olds (Table 2), with a significant difference between the two age groups ($p = 0.012$).

ROC curve analyses show that the optimal cutoff point for serum vitamin D concentrations at the end of summer to discriminate between sufficient and non-sufficient vitamin D at the end of the winter was 40 ng/mL. The area under the curve for 25(OH)D at the end of the summer was 0.70 (95% confidence interval: 0.58, 0.83; $p = 0.004$) (Figure 1).

Multiple log-binomial regression showed that sex, age and vitamin D status at the end of the summer (i.e. 25(OH)D: 30 to <40 ng/mL vs. ≥40 ng/mL) significantly predicted non-sufficient vitamin D at the end of winter. Children and adolescents with 25(OH)D in the range of 30 to <40 ng/mL at the end of the summer were 1.94 times more likely to be vitamin D-non-sufficient at the end of the winter compared with children and adolescents with 25(OH)D ≥40 ng/mL at the end of the summer. Compared with boys, girls were at higher risk of being vitamin D-non-sufficient at the end of the winter (Table 3).

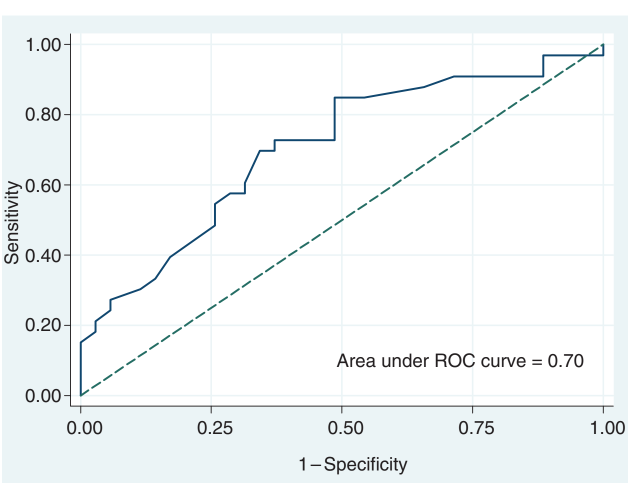

Figure 1: ROC curve for 25(OH)D at the end of the summer for discriminating between sufficient and non-sufficient vitamin D concentrations at the end of the winter.

Table 3: Multiple log-binomial regression to predict not-sufficient vitamin D_{winter} based on vitamin D_{summer} adjusted for sex and age.

	RR	95% CI for RR		p-Value
Sex				
Girl	1.59	1.14	2.22	0.006
Boy	1			
Age, years				
13–18	1.12	1.119	1.121	<0.001
7–12	1			
25(OH)D_{summer}, ng/mL				
30 ≤ 25(OH)D < 40	1.94	1.25	3.02	0.003
40 ≤ 25(OH)D	1			

CI, confidence interval; RR, relative risk; vitamin D_{summer}, serum vitamin D concentrations at the end of the summer; vitamin D_{winter}, serum vitamin D concentrations at the end of the winter.

Discussion

This study analyzed vitamin D concentrations in children and adolescents aged 7–18 years, with the results used to determine an adequate cutoff for serum vitamin D concentrations at the end of the summer. In most participants, vitamin D concentrations decreased from the end of the summer to the end of the winter, with a mean change of 15 ng/mL. This decrease was not significantly different in males and females, but mean vitamin D concentration decreases were more pronounced in adolescents 13–18 years old than in children 7–12 years old. The optimal cutoff for discriminating between sufficient and non-sufficient vitamin D concentrations at the end of winter was 40 ng/mL at the end of the summer.

To our knowledge, this is the first prospective study of vitamin D changes in children and adolescents with sufficient vitamin D levels from the end of the summer to the end of the winter. The strengths of our study include the longitudinal design which allowed us to collect data over time and minimize between-subject variability. In addition, our study used a very well-defined and healthy subject population. Subjects suffering from any systemic diseases, such as endocrine disorders, diabetes, renal or liver dysfunction, hyper/hypothyroidism and respiratory disease or calcium metabolism disorder, were excluded from the study [18], with participants undergoing a broad range of blood tests (calcium, phosphorus, 25(OH)D, parathyroid hormone and alkaline phosphatase) to ensure eligibility [18]. A valuable result of this study is the introduction of a cutoff point for vitamin D levels at the end of the summer to identify children and adolescents who are at risk of becoming vitamin-deficient.

Limitations of this study include the small cohort size. Due to funding constraints, only 68 participants out of a planned sample size of 113 participants were included in the study. Another limitation of the study is the absence of a control group. Careful consideration to include a control group was given during the designing of this study. Participants with vitamin D concentrations <30 ng/mL who were enrolled in the cross-sectional phase of the study could have been used as a control group. However, in accordance with the ethical principles of clinical research, which stipulate that subjects should not be denied beneficial treatments available, participants whose vitamin D concentrations were <30 ng/mL during the first part of the study were referred to an endocrinologist for diagnosis and treatment [18, 26].

Overall, our study revealed that insufficient concentrations of vitamin D in children and adolescents in winter is related to vitamin D concentrations in summer, sex and age. Several factors influencing vitamin D levels are reported in various studies, including reduced exposure to sunlight, reduced vitamin intake, age, sex and excess weight [27–31]. Findings that the body's capacity to synthesize vitamin D decreases with age [32] were confirmed in our study, where older participants (13–18 years old) had a greater reduction in vitamin D levels compared with younger participants (7–12 years old).

In this study, there was a greater reduction in the vitamin D concentrations in females compared to males (perhaps due to the female dress code in Iran). Although this reduction was not significant in our study, a correlation between vitamin D concentrations and sex is commonly reported in the literature [29, 31]. The relationship of vitamin D intake, serum vitamin D concentrations and exposure to UV-B radiation is well established in the literature [33, 34], with serum vitamin D concentrations increasing proportionally to UV-B exposure [35, 36]. In a study conducted in Brazil, the range of vitamin D concentrations in young and physically active subjects was the highest due to increased exposure to sunlight. Seasonal variations in vitamin D concentrations could be explained by the sinusoidal pattern of UV radiation [24]. Consequently, in order to maintain adequate vitamin D concentrations in winter, the human body has to synthesize vitamin D before the winter season or supplemental oral medication (vitamins) has to be taken. Although increasing sun exposure can enhance vitamin D concentrations, relying on increased UV radiation to increase vitamin D concentrations is not recommended. Studies have proven that exposure can lead to increased risks in cancer and skin burns [37]. Instead, some researchers have suggested resorting to consumption of vitamin D supplements, although this also has its limitations. A study by Anderson et al. [10] on 52 women and 54 girls (11–13 years) found that vitamin D intake either through diet or supplements is associated with vitamin D status but that seasonal changes have a greater impact on vitamin D concentrations, especially in children [38, 39]. In most cases, the amount of vitamin D available through food sources is not sufficient and access to nutritional supplements is limited, thus explaining the prevalence of vitamin D deficiency even in European countries and in the US [40]. In a study conducted in 2011, Holic et al. [41] found that if vitamin D concentrations during the summer were below 20 ng/mL (considered a vitamin D deficiency), vitamin D supplements could be a therapeutic strategy to improve vitamin D concentrations in winter. This team also concluded that in order to maintain vitamin D concentrations of 20 ng/mL throughout the winter, sunlight exposure should be increased during the summer or vitamin D supplements should be taken. The results of our study showed that subjects with summer vitamin D concentrations between 30 and 40 ng/mL were 1.94-fold more likely to be vitamin D-non-sufficient than subjects who had vitamin D concentrations >40 ng/mL in the summer. Our study, which was conducted in northeastern Iran, also found that vitamin D concentrations >40 ng/mL provided an assurance of vitamin D sufficiency at the end of the winter. Finally, another study team found that to maintain vitamin D concentrations of 15.7 ng/mL (50 nmol/L) in winter, summer vitamin D concentrations should be about 31.4 ng/mL (100 nmol/L) and that if the summer vitamin D concentrations were about 18.9 ng/mL (60 nmol/L), then the winter vitamin D concentrations would approximately be 8.8 ng/mL (28 nmol/L), which corresponds to vitamin D insufficiency [10].

Conclusions

We found that sufficient vitamin D concentrations (25(OH)D ≥30 ng/mL) at the end of summer cannot guarantee sufficient vitamin D concentrations for the winter season. However, a cutoff of 40 ng/mL for 25(OH)D at the end of summer may provide assurance of vitamin D sufficiency throughout the winter in subjects aged 7–18 years in our geographic location (northeastern Iran). We also found that the average vitamin D concentration decreases were more pronounced in subjects aged 13–18 years. In this context, we believe that medical attention should be given to this age group to prevent inadequate vitamin D concentrations and resulting ailments. Further studies on factors contributing to vitamin D concentration decreases should be conducted in a larger group of subjects.

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