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Trabajo Original

Pediatría

The association between 25-hydroxyvitamin D levels and muscle strength in adolescents

La asociación entre los niveles de 25-hidroxivitamina D y la fuerza muscular en los adolescentes

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Abstract

Background: since the discovery of the vitamin D receptor in muscle cells, relatively few studies conducted in adolescents have reported with conflicting results the relationship between serum 25-hydroxyvitamin D [25(OH)D] levels and muscle strength.

Methods: the National Health and Nutrition Examination Survey during the period 2011-2014 was analyzed to examine the association between vitamin D status and the combined maximum grip strength, as a proxy for overall muscle strength in participants aged 10 to 19 years. According to the American Endocrine Society guidelines, subjects with 25(OH)D levels < 20 ng/mL, 20 to 30 ng/mL, and > 30 ng/mL were defined as having deficient, insufficient, and sufficient vitamin D, respectively. General linear models were assembled to examine this association.

Results: of 2,528 participants with a mean age of 14.5 years, the prevalence of vitamin D deficiency and sufficiency was 25.6 % and 25.9 %, respectively. As expected, maximum grip strength increased with age and was stronger in boys than that in girls. Notably, after adjusting for potential confounders, boys and girls with vitamin D sufficiency were on average 2.9 kg and 2.1 kg stronger than their counterparts with vitamin D deficiency, respectively. Moreover, boys defined as having severe vitamin D deficiency (< 12 ng/mL) were 4.1 kg weaker than those who did not.

Conclusion: in adolescents, vitamin D sufficiency was significantly associated with stronger combined maximum grip strength. The present findings should be further investigated to determine if maintaining optimal 25(OH)D concentrations might result in greater muscle strength in adolescents.

Keywords:

Adolescents. Vitamin D. Muscle strength.

Resumen

Antecedentes: desde el descubrimiento del receptor de la vitamina D en las células musculares, relativamente pocos estudios realizados en adolescentes han reportado, con resultados contradictorios, la relación entre los niveles séricos de 25-hidroxivitamina D [25(OH)D] y la fuerza muscular.

Métodos: la Encuesta Nacional de Salud y Nutrición durante el periodo 2011-2014 se analizó para determinar la relación entre los niveles séricos de 25(OH)D vitamina D y la fuerza de agarre máxima combinada, usada como un aproximado de la fuerza muscular general, entre participantes de edades comprendidas entre los 10 y los 19 años. De acuerdo con las directrices de la Sociedad Americana de Endocrinología, los participantes con niveles de 25(OH)D < 20 ng/ml, de 20 a 30 ng/ml y > 30 ng/ml se definieron como deficiencia, insuficiencia, y suficiencia de vitamina D, respectivamente. Modelos generalizados lineales ajustados por cofactores se usaron para examinar esta asociación.

Resultados: de 2528 participantes con una edad promedio de 14,5 años, la prevalencia de la deficiencia y la suficiencia de vitamina D fue del 25,6 % y del 25,9 %, respectivamente. Como era de esperar, la fuerza máxima de agarre aumentó con la edad y fue más fuerte en los niños que en las niñas. En general, los niños y niñas con suficientes niveles de 25(OH)D fueron en promedio 2,9 kg y 2,1 kg más fuertes que sus homólogos con deficiencia de vitamina D, respectivamente. Además, los niños con deficiencia severa de vitamina D (< 12 ng/ml) fueron en promedio 4,1 kg más débiles que los que no la tenían.

Conclusión: en adolescentes, los niveles suficientes de vitamina D se asociaron a una mayor fuerza de agarre máxima combinada. Los hallazgos actuales deben investigarse más a fondo para determinar si mantener niveles óptimos de 25(OH)D podría resultar en una mayor fuerza muscular en los adolescentes.

Palabras clave:

Adolescentes. Vitamina D. Fuerza muscular.

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INTRODUCTION

Osteomalacia is characterized by abnormal matrix mineralization in established bone, and although present in children with rickets, it is used to describe bone mineralization defects after completion of growth (1). Myopathy manifested as proximal muscle weakness affecting the lower extremities has been described as a prominent feature of osteomalacia, which may be present even before biochemical signs of bone disease (2-3). Moreover, since the discovery of the vitamin D receptor in human muscle cells, studies conducted particularly among older adults have reported with conflicting results the relationship between 25-hydroxyvitamin D (25(OH)D) levels and muscle strength (4). Although some observational studies demonstrated a positive correlation between 25(OH)D levels and muscle strength (5-9), others did not (10-11). Despite these facts, relatively few studies have explored the relationship between vitamin D status and muscle strength in adolescents.

Previously, a cross-sectional study conducted in Chinese girls aged 12 to 15 years reported that serum 25(OH)D concentrations ≥ 20 ng/mL were associated with greater grip strength (12). Likewise, in the Young Hearts Study, boys 15-year-old with serum 25(OH)D levels > 20.4 ng/mL had significantly greater grip strength (GS) than those with 25(OH)D levels < 12.8 ng/mL. However, in the latter study, GS did not significantly differ across 25(OH)D levels among girls and 12-year-old boys (13). Given that muscle strength correlates with bone mass acquisition during adolescence, it is relevant to determine the effect of 25(OH)D levels on muscle strength during this critical period of musculoskeletal growth (14). Therefore, the present cross-sectional study aimed to examine the relationship between vitamin D status and grip strength in a nationally representative sample of adolescents.

METHODS

STUDY POPULATION

The present cross-sectional analysis was based on data from participants aged 10 to 19 years in the continuous National Health and Nutrition Examination Survey (NHANES) 2011-2012 and 2013-2014 cycles. The NHANES is designed to assess the health and nutritional status of adults and children in the United States (USA). A complex, multistage probability sampling design was used to select a sample representative of the civilian non-institutionalized household population of the USA. The NHANES protocol was approved by the National Center for Health Statistics Research Ethics Review Board (study protocol # 2011-17). An informed consent was obtained from those who had reached the age of maturity in their State. A parent or guardian gave permission for minors to participate (15).

Characteristics of participants

Age, sex, and race/ethnicity were self-reported. The household reference person described the highest level of education obtained, and the ratio of family income to poverty was calculated as a measure of family's poverty status. In the interview file, sedentary lifestyle over the past 30 days was assessed by asking participants "How many hours per day did you sit and watch TV or videos? Self-reported general health was grouped as good to excellent and fair to poor. In the dietary interview component, participants' daily total protein intake was reported in grams. Standing height (cm) was measured using a stadiometer and a fixed vertical backboard. Moreover, participants' total percent fat mass and total lean mass (g), excluding bone mineral content, were measured using whole-body scans densitometers (Hologic, Inc., Bedford, Massachusetts, USA).

Vitamin D status

Total 25-hydroxyvitamin D (25(OH)D) is the predominant circulating form of vitamin D and is considered to be the most reliable index of vitamin D status. Total 25-Hydroxyvitamin D is the sum of 25-hydroxyvitamin D_2 and 25-hydroxyvitamin D_3, but excludes epi-25-hydroxyvitamin D_3. The ultra-high performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) method was used for the quantitative detection of serum 25(OH)D. A complete description of the laboratory procedure manual is available at: https://wwwn.cdc.gov/nchs/data/nhanes/2011-2012/labmethods/VID_G_met_Vitamin_D.pdf.

For this analysis, 25(OH)D level in nmol/L was converted to ng/mL (1 nmol/L = 0.4 ng/mL). According to the American Endocrine Society guidelines, adolescents with 25(OH)D levels < 20 ng/mL were defined with vitamin D deficiency, those with 25(OH)D levels between 20 and 30 ng/mL represented vitamin D insufficiency, and those with 25(OH)D levels > 30 ng/mL were considered as having vitamin D sufficiency (16). Moreover, as indicated by the Institute of Medicine, subjects with serum 25(OH)D levels < 12 ng/mL were at risk of deficiency relative to bone health (17).

Muscle strength

A detailed description of the muscle strength procedure manual is available at https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/muscle_strength_2013. Briefly, muscle strength was measured using a handgrip dynamometer. Participants, while standing, squeezed the dynamometer as hard as possible. The exam was then repeated in each hand three times, with a 60-second rest between trials on alternating hands. The combined maximum GS, expressed in kilograms (kg) was calculated as the sum of the greatest reading for each hand. Those who were unable to hold the dynamometer with both hands or had any surgery in the hands/wrists in the prior 3 months were excluded for this analysis.

STATISTICAL ANALYSIS

The characteristics of participants were compared across vitamin D status using the Chi-squared and ANOVA tests for categorical and continuous variables, respectively. Sex-specific general linear models were assembled to examine the association between vitamin D status and combined maximum GS. The following covariates were included in the multivariate models: model 1 was adjusted for age and height, and model 2 was further adjusted for race/ethnicity, household reference person's education, ratio of family income to poverty, hours of sedentary lifestyle, self-reported health, total fat mass percent, total lean mas, and daily protein intake. The SPSS Complex Sample software, v.25 (SPSS Inc, Chicago, Illinois, USA) was used in all analyses to account for the NHANES complex survey design. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 2,528 adolescents with a mean age of 14.5 (SE: 0.07) years comprised the study sample. Table I shows the characteristics of participants stratified according to vitamin D status. In general, girls, non-Hispanic black, low income, higher total percent fat mass, sedentary lifestyle, and lower protein intake were characteristics associated with vitamin D deficiency. Overall, vitamin D deficiency, insufficiency, and sufficiency were prevalent in 25.6 %, 48.5 %, and 25.9 % of participants, respectively. Moreover, 4.1 % of adolescents were defined at risk of vitamin D deficiency relative to bone health. As shown in figure 1, the combined maximum GS was similarly distributed in both sexes among participants aged 10 to 12 years. Thereafter, GS progressively increased in boys, reaching a maximum strength of 88.7 kg at the age of 19 years. In girls, the increase in GS was less accentuated. However, between the ages of 13 and 19 years, GS increased by 9.8 kg in girls.

Table II shows the combined maximum GS stratified according to vitamin D status and sex. As expected, boys were consistently stronger than girls regardless of their vitamin D status. Notably, after adjusting for potential confounders, the combined maximum GS was on average 2.9 kg higher among boys with vitamin D sufficiency than their counterparts with vitamin D deficiency. Similarly, girls with vitamin D sufficiency were 2.1 kg stronger than those with vitamin D deficiency. Moreover, boys defined as having severe vitamin D deficiency were 4.1 kg weaker than those who did not. However, muscle strength did not significantly differ between girls with or without severe vitamin D deficiency (Table III). In a subgroup analysis, participants aged 15 to 19 years were con-

Table I. Characteristics of participants according to vitamin D status

	< 20 ng/mL (n = 949)	20 to 30 ng/mL (n = 1,185)	> 30 ng/mL (n = 394)	p-value
Age (years), mean	14.9 (0.1)	14.2 (0.1)	14.6 (0.2)	< 0.05
Gender, %				< 0.05
Boys	22.9 (2.3)	52.1 (2.1)	25.0 (2.6)	
Girls	28.5 (2.3)	44.6 (2.3)	26.9 (3.3)	
Race/ethnicity, %				< 0.0001
Hispanic	39.5 (3.5)	50.4 (3.0)	10.1 (1.4)	
Non-Hispanic white	9.7 (1.4)	50.9 (2.8)	39.4 (3.4)	
Non-Hispanic black	63.3 (2.6)	33.1 (2.3)	3.7 (0.8)	
Non-Hispanic Asian	43.6 (3.9)	48.5 (3.7)	7.9 (1.4)	
Other race	23.0 (5.6)	55.0 (6.8)	22.0 (6.7)	
HH reference person's education, %				< 0.0001
< 9th grade	41.2 (4.2)	49.0 (4.2)	9.8 (4.0)	
9th to 11th grade	33.7 (2.5)	51.4 (2.5)	14.9 (3.0)	
High school graduate	31.6 (3.0)	46.3 (3.6)	22.1 (4.1)	
Some college	23.0 (2.5)	49.6 (3.1)	27.3 (2.7)	
College graduate	15.7 (2.3)	45.7 (2.4)	38.6 (3.7)	
Ratio of family income to poverty, mean	1.9 (0.08)	2.4 (0.1)	2.9 (0.1)	< 0.0001
Standing height (cm), mean	162.4 (0.48)	162.0 (0.62)	162.8 (0.75)	0.778
Fat mass (%), mean	31.6 (0.3)	29.9 (0.3)	28.0 (0.4)	< 0.0001
Lean mass (g), mean	43,503.6 (591)	41,570.0 (586)	40,200.7 (611)	< 0.001
Sedentary lifestyle (hours), mean	5.5 (0.1)	4.4 (0.1)	4.1 (0.1)	< 0.0001
Self-reported health, %				
Good to excellent	24.4 (2.0)	48.8 (1.6)	26.8 (2.6)	< 0.0001
Fair to poor	47.3 (4.6)	41.5 (4.4)	11.2 (3.8)	
Protein intake (g), mean	71.2 (1.5)	78.6 (1.6)	80.9 (3.7)	< 0.05

HH: household. Parenthesis represents standard error of the estimate.

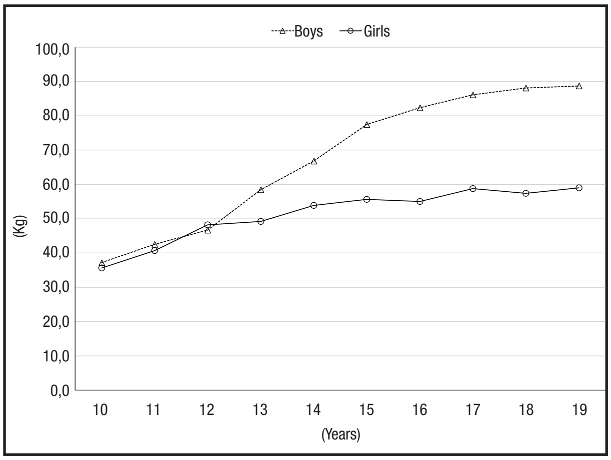

Figure 1.

Mean combined maximum grip strength according to age and sex in adolescents.

Table III. Combined maximum grip strength in adolescents according to severe vitamin D deficiency and sex

	25(OH)D levels			
	< 30 nmol/L	≥ 30 nmol/L	Mean difference	p-value
Boys (kg)				
Model 1	66.7 (0.6)	68.3 (0.6)	-1.6 (1.9)	0.411
Model 2	64.3 (1.6)	68.4 (0.4)	-4.1 (1.7)	< 0.05
Girls (kg)				
Model 1	52.8 (0.9)	51.2 (0.3)	1.6 (1.0)	0.124
Model 2	50.6 (1.0)	51.0 (0.3)	-0.4 (1.1)	0.701

Model 1: adjusted for age and standing height. Model 2: adjusted for model 1 and race/ethnicity, reference person's education, ratio of family income to poverty, sedentary lifestyle, self-reported health, total fat mass percent, total lean mass, and protein intake.

Table II. Combined maximum grip strength in adolescents according to vitamin D status and sex

25(OH)D levels	< 50 nmol/L (reference)	50 to 75 nmol/L	> 75 nmol/L
Boys (kg)			
Model 1	67.8 (0.7)	68.6 (0.9)	68.0 (1.1)
Model 2	66.4 (0.6)	68.5 (0.8)	69.3 (0.7)*
Girls (kg)			
Model 1	52.0 (0.6)	50.7 (0.5)	51.7 (0.6)
Model 2	50.3 (0.4)	50.6 (0.5)	52.4 (0.5)*

**p-value < 0.05 compared with category < 50 nmol/L. Model 1: adjusted for age and standing height. Model 2: adjusted for model 1 and race/ethnicity, reference person's education, ratio of family income to poverty, sedentary lifestyle, self-reported health, total fat mass percent, total lean mass, and protein intake.*

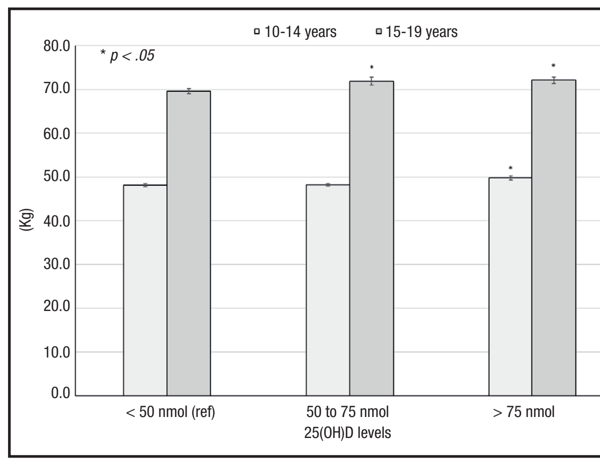

Figure 2.

Combined maximum grip strength according to vitamin D status and age groups.

siderably stronger than their younger counterparts, irrespective of their vitamin D status. However, according to age group, a similar difference in GS (1 kg) was seen between participants with vitamin D sufficiency and those with vitamin D deficiency (Fig. 2).

DISCUSSION

The results of this cross-sectional study indicate that vitamin D status was significantly associated with muscle strength in adolescents. Notably, boys and girls with vitamin D sufficiency were significantly stronger than their counterparts with vitamin D deficiency. Moreover, boys at risk of vitamin D deficiency (< 12 ng/mL) relative to bone health were on average 4.1 kg weaker than those at no such risk. As expected, the combined maximum GS among adolescents markedly increased from age 12 years onward and boys were stronger than girls. The differences in muscle strength between age groups and sexes among adolescents have been explained by an age-dependent increase in fat-free mass and the anabolic effect of testosterone after puberty in boys (18,19). Nevertheless, even after adjusting for body composition, adolescents aged 15 to 19 years with vitamin D insufficiency and sufficiency were significantly stronger than those with vitamin D deficiency.

The present findings are consistent with those reported in a cross-sectional study among Chinese adolescent girls aged 15 years, in which participants with 25(OH)D levels ≥ 20 ng/mL had on average 1.8 kg greater GS than their counterparts with a poor vitamin D status (12). Similarly, in the Young Hearts Study, boys 15-year-old with 25(OH)D levels > 20.4 ng/mL had on average 3.8 kg stronger GS than those with 25(OH)D levels < 12.8 ng/mL (13). In addition, among girls in the HELENA study and a small study conducted among Ethiopian school children, serum 25(OH)D levels were significantly correlated with GS (20,21).

In contrast, a 7-year longitudinal study among girls aged 10 to 13 years recruited from schools in Central Finland reported no differences in muscle strength between participants with 25(OH) D levels < 20 ng/mL and those with higher 25(OH)D levels (22). Likewise, previous clinical trials designed to determine the beneficial effect of vitamin D supplementation on muscle strength have reported negative results. For instance, a small placebo-controlled study conducted among British men with a mean age of 22.7 years reported that participants supplemented with vitamin D 10,000 IU/day for 12 weeks achieved 25(OH)D levels > 48 ng/mL. However, these 25(OH)D concentrations did not improve the peak torque for maximal extension and flexion of the lower limbs as compared with the placebo group (23). Among Asian Indian females with a mean age of 21.7 years and a high prevalence of vitamin D deficiency at baseline, cholecalciferol 60,000 IU/week for 2 months, and then 60,000 IU twice per month for 4 months did not significantly increase grip strength at the end of the trial (24). Possible reasons for these contradictory results may be related to the age of participants, race/ethnicity, sample size, and a high prevalence of participants with vitamin D deficiency at baseline.

Although the physiological effects of vitamin D on muscle strength have not been completely elucidated, it was reported that 1,25-dihydroxyvitamin D_3 increases calcium influx in muscle cells and may have a role in the regulation of muscle cell cytoskeleton protein synthesis (25). Moreover, Girgis et al. demonstrated that mice with deletion of the vitamin D receptor or diet- induced vitamin D deficiency were weaker than controls (26). Notably, cholecalciferol therapy has demonstrated to improve muscle mitochondrial maximal phosphorylation after exercise in individuals with severe vitamin D deficiency, which may partially explain the myopathy experienced by these subjects (27).

The present study has some limitations that should be mentioned. First, because of its cross-sectional design, the temporal relationship between vitamin D status and combined maximum GS may not be established. Second, the hand-grip strength was used as a proxy for overall muscle strength. However, unadjusted and weight-adjusted hand-grip strength has been reported to have a strong and moderate correlation with other muscle groups in children and adolescents, respectively (28). Whether vitamin D status has similar effects on total muscle strength among adolescents is uncertain. Third, although 25(OH)D cutoff levels defining vitamin D status were developed relative to bone health, it appears that vitamin D status may also be used to identify adolescents with muscle weakness. Finally, data on the participants' pubertal status and sex hormone levels were not included in this analysis. Despite these limitations, the study findings may be generalized to the adolescent population in the U.S.

CONCLUSION

In conclusion, vitamin D sufficiency was significantly associated with stronger combined maximum grip strength in adolescents. In contrast, boys with severe vitamin D deficiency were considerably weaker than their counterparts without deficiency. The present findings should be further explored to determine if maintaining optimal 25(OH)D levels might result in greater muscle strength in adolescents.

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