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Research Article

Randomized Vitamin D Supplementation in Vitamin D Deficient Obese Children from West Virginia

Abstract

Objective: Vitamin D (Vit D) deficiency is a very common problem in obese children, but clinical guidelines for maintenance or treatment have not been published for this population. The aim was to assess the benefit of 2 months Vit D supplementation given to deficient obese children from WV.

Design: Vit D deficient obese children were prospectively recruited. Exclusion criteria included <8 years, and medical conditions that may affect Vit D homeostasis. Participants were randomized into two supplement groups: 5,000IU/day (Group A) or 50,000IU/week (Group B). Serum 25(OH)D levels were measured at baseline and post-treatment.

Results: Sixty obese children were screened of whom 39 (65%) were deficient (<20ng/ml). Of the 39 recruited, 26 completed the study. The mean serum 25(OH)D after 2 months treatment were significantly higher in Group B (p= 0.02), but most reached normal levels (>30ng/ml).

Conclusions: Two months Vit D supplementation (5000IU/day or 50,000IU/week) was sufficient to normalize 25(OH)D levels in Vit D deficient obese West Virginian children.

Abbreviations

(Vit D): Vitamin D; (RDA): Recommended Dietary Allowances; (ESPGHAN): European Society of Pediatric Gastroenterology Hepatology and Nutrition; (25(OH)D): Serum Vit D levels; (Group A): Daily dose 5,000IU Vit D: (Group B): Weekly dose 50,000IU Vit D given as a single dose; (IRB): Institutional Review Board; (AA): African American

Background

Vitamin D (Vit D) plays a crucial role in the development of musculoskeletal growth in children and its role in other systems has also been recognized including the immune system, endocrine system (diabetes, obesity), infection, and other conditions [1-4]. Vit D can be acquired by children through sun exposure, specific foods with high Vit D content and/or foods supplemented with Vit D, or direct supplementation. Obesity and Vit D deficiency are known epidemics throughout the world [5]. In a large report, high rates of Vit D deficiency were documented in American children, and several high risk factors were identified including: obesity, ethnicity, female gender, and sun exposure time [6]. To date, the published Recommended Dietary Allowances (RDA) of Vit D for normal, healthy children, have been found insufficient for those children belonging to those high risk groups [6]. In a recent review of the subject, the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guideline on Nutrition recognized that children with high risk conditions were not specifically addressed, and allowed for Vit D dose changes depending on local circumstances in different communities [7]. Others recommended following Vit D serum levels (25(OH)D) every 6 months in order to prevent deficiency in children [8]. The current RDA for normal weight healthy children older than 8 years is 3,000IU-4,000IU/day and normal serum 25(OH)D is defined as >30ng/ml [7,9,10].

The obesity rate in children living in West Virginia was reported as one of the highest in the United States [11]. Obesity has been recognized as a major high risk condition for Vit D deficiency in children, but no official RDA or recommended therapeutic dose for Vit D deficient obese children have been published. Consequently, in the present study, we investigated the efficacy of Vit D supplementation in deficient obese children

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from West Virginia. We compared the serum 25(OH)D levels after 2 months supplementation of daily 5,000IU (Group A) Vit D or weekly 50,000IU Vit D given as a single dose (Group B).

Materials and Methods

Patient population

We have calculated that the number of patients needed is > 40 children (estimated sample size when alpha-0.05, power-80%, delta-0.19). Accordingly, we prospectively screened 60 obese children who attended the Pediatric Gastroenterology clinic for various clinical symptoms. Exclusion criteria included children <8 years, inability to swallow pills, and the following medical conditions: hypercalcemia, mal-absorption syndromes (celiac disease, cystic fibrosis, IBD), endocrine diseases that affect Vit D or calcium homeostasis (hypo/hyperthyroidism), diseases or medications that affect bone metabolism (steroids), or diseases that may affect the immune system (immunosuppressive meds, biologic medications) [12,13]. Obesity was defined according to the CDC BMI chart (>95%tile). Children with Vit D deficiency (< 20ng/ml), who met the eligibility criteria, were prospectively recruited. Serum 25(OH)D levels were taken again at the end of the study. The subjects and their parents/legal guardians signed consent forms provided by the research coordinator before participation. The study was approved by the Institutional Review Board (IRB) at Marshall University School of Medicine.

Vit D supplementation

As RDA doses of Vit D supplementation for Vit D deficient obese children have not been published we carefully chose 2 different doses of Vit D for this study based on previous studies and guidelines published on Vit D deficient normal weight children. The lower dose (5,000IU/day) was chosen because the RDA of Vit D for normal weight children >8 y/o (4,000IU/day) was insufficient to maintain adequate serum levels (>30ng/ml) in over 20% of them [6]. The higher dose (50,000IU/week) was chosen as it was recommended by the Endocrine Society's practice guidelines for normal weight children, and was successfully used in Vit D deficient children with chronic diseases [10,14,15]. The study period was assigned 8 weeks as previous data showed that it was safe [7,10,14,15]. The study's primary outcome was to investigate the success rate of each dose to achieve normal serum levels after 2 months of supplementation. The secondary outcome was to assess the compliance rate between both modes of administration (daily vs. weekly).

Study protocol

Vit D Deficient obese children were assigned, based on a computer generated randomization, to one of two different oral doses of Vit D supplementation: a pill of 5,000IU every day (Group A) or 10 pills of 5000IU each (total 50,000IU) once weekly (Group B) [16]. Participants were provided with gel capsules of Vit D (5,000IU/capsule). Compliance was secured through weekly telephone confirmations and pill counts performed at the 1 and 2 month clinic visits. Serum levels of 25(OH)D were checked at baseline and post-treatment and were compared.

Statistical analysis

Statistical analyses were performed using GraphPad Prism for Windows version 6.02 (GraphPad Software, Inc. La Jolla, CA). A non-parametrical test (Mann Whitney test) was used to assess the difference between the groups. A one way ANOVA was used to assess the differences between the mean seasonal data. Chi-square analysis was used to determine the differences in the compliance data.

Results

Serum levels of 25(OH)D were examined in 60 obese children between October 2013 and April 2015 of whom 39 (65%) were Vit D deficient (<20ng/ml). Of the 39 eligible children, 10 declined participation and 3 were omitted due to protocol violations (incomplete treatment: 2 from Group A, 1 from Group B). Accordingly, a total of 26 eligible children (14 - Group A, 12 - Group B) constituted our study population. All participants were Caucasians and no significant difference in the mean age was observed between the groups (Table 1). Mean Vit D levels post-treatment were significantly lower in Group A compared to Group B (p = 0.027), but both groups' averages were within the defined sufficient levels (>30ng/ml) (Table 1). None of the participants reached Vit D toxicity levels post-therapy (> 150ng/ml).

The seasonal distribution of Vit D (mean ± SD) levels observed in the 60 children at baseline showed the following results: Winter (December-February) - 17.1 ± 3.0ng/ml (6 children); spring (March-May) - 16.4 ± 2.8(ng/ml) (12 children); summer (June-August) - 25.2 ± 10.7ng/ml (11 children); and fall (September-November) - 19.6 ± 7.1ng/ml (31 children). Vit D levels were significantly higher during the summer season compared with all other seasons (p = 0.0252). The compliance rate was similar in both groups (87.5% in Group A vs. 92.3% in Group B; p = 0.6725) (Table 1).

Table 1: Vitamin D supplementation in obese children.

Vit D	# Patients Comp. Tx	M:F	Age (y) ±SD	Compliance Rate (%) (Comp. Tx/Total Pts)	Initial 25(OH)D(ng/ml) (Mean ± SEM)	Final 25(OH)D(ng/ml) (Mean ± SEM)
Group A (5000IU/day)	n=14	9:5	12 ±2.8	87.5 (14/16)	15.06 (± 3.596)	39.50 (± 2.861)
Group B (7500IU/day) (given as a single dose weekly)	n=12	4:8	11 ±2.6	92.3 (12/13)	16.63 (± 1.890)	50.32 (±4.091)
p-value			0.3786	0.672	0.187	0.027

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The RDA of Vit D and/or the optimal therapeutic dose for obese children who are Vit D deficient have not been reported. In the present study we showed that a weekly dose of 50,000IU for 2 months achieved a higher mean serum level of 25(OH) D compared to a daily dose of 5,000IU (50.32 ± 4.09 vs. 39.50 ± 2.86; p = 0.0269). In spite of the difference in the average dose of daily Vit D (7,500IU/d vs. 5,000IU/d), both doses were sufficient to achieve normal levels (>30ng/ml). As expected, none of our patients reached toxicity levels (> 150ng/ml). The handful of pediatric cases reported with Vit D toxicity suggested that the supplementation dose associated with toxicity is much higher (factor of >100) than the doses used in our study [17-19]. Consequently, under our study's conditions, Vit D toxicity was very unlikely.

Discussion

Obesity rates in children from West Virginia were reported as one of the highest in the United States [11]. Obesity has been recognized as a major risk factor for Vit D deficiency [6]. Unfortunately, the status of serum Vit D levels in West Virginian children has not been well studied. In a single study, Robinson C et al. [20], assessed Vit D status in West Virginian children who were referred to their endocrine clinic. The study showed that 23.7% of the cohort were Vit D deficient (<20ng/ml) and that obesity was significantly associated with Vit D deficiency [20]. The efficacy of Vit D supplementation was not examined in that study.

The association between obesity and Vit D deficiency has been well established but whether there is a causal relationship is unknown. It was suggested that the reason for lower Vit D levels in obese subjects is related to the slow release of Vit D from the skin into the circulation [20]. Moreover, an inverse correlation was found between Vit D levels and BMI after oral intake of Vit D or when radiation (sun exposure) was the source of supplementation [20]. Nonetheless, the regulatory interaction between obesity and Vit D deficiency is not known [5]. Some suggested that Vit D deficiency precedes obesity in adults, while in a pediatric study from the Brazilian Amazon showed that the obesity related gene (FTO rs9939609) was more pronounced in Vit D deficient children [22,23]. In a bidirectional Mendelian randomization analysis it was concluded that obesity is a causal factor in the development of Vit D deficiency but not vice versa (24).

Specific reports on the efficacy of Vit D supplementation in Vit D deficient obese children are very limited. In an unpublished study, Kelly et al. compared a daily dose of 1,000IU/day vs. 5,000IU/day Vit D supplementation in obese African American (AA) children for 3 months [25]. At the end of the study only 50% of the 5,000IU supplemented group and none from the lower dose group (1000IU/day) reached normal serum 25(OH) D levels (>30ng/ml). In our study, only 2 (14%) children from Group A did not reach adequate serum levels after 2 months supplementation. AA ethnicity has been established as a high risk for Vit D deficiency in children. Some investigators implicated skin pigmentation, differences in intestinal absorption, or racial variances in the endocrine system as factors that reduce Vit D production in AA [6,21,26,27]. Although those factors were not examined in our study, they may explain the different success rates noted between our study (Caucasian patients) and Kelly's study (AA patients) who received the same daily doses of Vit D supplementation (5,000IU/day) [25].

We acknowledge the following limitations in our study; (a) the study included a small number of participants and was limited to 2 months of supplementation. A larger and prolonged study (>6 months) might have resulted in different Vit D levels in both groups. (b) Other sources of Vit D supplementation were not measured including sun exposure and dietary intake. Nonetheless, the Vit D supplementation given to the study participants was much higher than the children's average daily Vit D intake through their diet or via sun exposure (http://dietarysupplementdatabase.usda.nih.gov; [28]), (c) Several known risk factors for Vit D deficiency could not be assessed in the present study including gender and ethnicity. Accordingly, we conclude that our results are limited to obese Caucasian children from West Virginia and cannot be extrapolated to other pediatric populations. Future larger pediatric studies that include different ethnicities and gender variability are clearly warranted.

Conclusions

In summary, there are no guideline recommendations to prevent or treat Vit D deficiency in obese children. In the present study we investigated the efficacy of two Vit D supplementation doses, 5,000IU/day vs. 50,000IU/week, in Caucasian Vit D deficient obese children. We concluded that after 2 months, both doses were adequate to achieve normal serum 25(OH)D levels. Future larger studies will be needed to substantiate our results.

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