

Research Article

Vitamin D3 Supplementation to Children; A Pilot-Study of Adherence

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Received: 30 June 2019; **Accepted:** 01 October 2019; **Published:** 03 October 2019

Citation of this article: Ekbom, K. (2019) Vitamin D3 Supplementation to Children; A Pilot-Study of Adherence. J Clin Nutr Food Sci, 2(2): 068-067.

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ABSTRACT

Background: Non-adherence to supplementation is a widespread public health problem and according to the World Health Organization adherence among patients with chronic disease averages is only 50 percent.

The difficulties in treating children with obesity are well-known and the outcome is highly dependent on adherence.

Obesity is associated with a low vitamin D₃ status and it is discussed if supplementation should be considered for obese children, when low vitamin D₃ status increases the risk of several diseases.

Objectives: The study aim was to determine the convergence between self-reported adherence and serum 25(OH)D₃ levels, the circulating vitamin D₃ metabolite.

Thereafter to compare the adherence between children with obesity vs normal-weight children.

Method: The study design was a prospective longitudinal study of 20 children (11-17 year of age) with a low vitamin D₃ status. The children were recommended supplementation for 2 months. Adherence was checked during visits at the clinic in combination with blood-sampling (25(OH)D₃).

Results: All the participants had a high self-documented adherence (75%), which was in line with the vitamin D₃ levels that increased significantly after 2 months. No difference was seen in the adherence between obese and normal-weight children.

Conclusion: The convergence between self-reported adherence and serum 25(OH)D₃ levels was high. The adherence to vitamin D₃ supplement for children works well due to frequent contacts with a pediatric nurse in combination with blood sampling with no difference between obese or normal-weight children.

Keywords: Adherence, Vitamin D₃, Obesity, Supplementation, Paediatric practice

Introduction

It is well-known that skin exposure to sunlight is the main source of vitamin D (D₃) production, with the skin synthesis of D₃ representing the first step of a metabolic pathway [1]. Thus,

it is relatively new knowledge that the vitamin D receptor and the activation enzyme CYP27B1 have been identified in a numerous cell types, suggesting involvement in a number of body function other than rickets in children and osteomalacia in adults [2].

In addition to the classical way of vitamin D₃ production, previous studies have shown that numerous pathways for metabolism of Vitamin D₃ exist [3], with the production of at least 40 metabolites whose role is only partially known [4]. In fact, low Vitamin D₃ status decreases the capacity of most tissues to transmit normal physiologic functions [5].

D₃ deficiency during childhood has been associated with infections and autoimmune diseases and increased risk of developing type 1 diabetes, later in life [6]. Some studies have also suggested that D₃ is associated with depression and some neuropsychological diagnoses [7,8].

D₃ supplementation is the treatment strategy for children with low levels of 25-Hydroxyvitamin D₃ (25(OH)D₃), the main circulating vitamin D₃ metabolite commonly used as the marker of D₃ status [9]. It is well established that obesity is associated with low levels of 25(OH)D₃ and it has been proposed that levels of 25(OH)D₃ are low, due to increased accumulation in the adipose tissue [10]. But there is no consensus as to why 25(OH)D₃ levels are decreased in obese individuals.

In this study we used the definition from the US Institute of Medicine (IOM); a value for 25(OH)D₃ above 50 nmol/L regarded as adequate (a lower safe reference limit) and values <30nmol/L as deficient and 25(OH)D₃ 30-50nmol/L as insufficiency [11].

In Sweden an intake of 400 IE is recommended with no supplementation, which is in line with the definition from the IOM recommendation [11]. However, some studies have recommended that D₃ supplementation should be increased to 2.000 IE per day [12] and some have studied the efficacy and safety of 4.000IE D3/d (IOM Tolerable Upper Intake Level) [13].

It is also discussed if children and adolescents with obesity should be recommended D₃ supplementation and if there is a need for higher doses of D₃ to achieve adequate levels of 25(OH)D₃ [14]. We have previously concluded that D3 supplementation should be considered for obese children living in Sweden [15] when the combination of obesity and low sunshine effectivity may severely affect obese children and adolescents D₃ status [12].

In this study we will highlight the adherence to recommended or prescribed supplementation when treating children and adolescents with obesity.

“Adherence is the extent to which a person’s behaviour in taking medication corresponds with agreed recommendations from health care provider” [16]. However, several studies have reported that adherence to different treatments is approximately 50% and that the outcome of the obesity management highly dependent on adherence [17].

Studies measuring adherence to vitamin recommendations defined adherence in variety ways with a majority relied on self-reported data [18].

Just a few studies have used serum levels of 25(OH)D₃ as a proxy for self-reported adherence to vitamin D supplementation making it difficult to determine if there is a convergence between self-reported adherence and D₃ status [19].

The difficulties in treating children with obesity are well known and the adherence to different behavior treatments including diet and

physical activities is poor [20]. We don’t know if there is a difference in adherence to supplementation between children with obesity and normal-weighted children. However, measuring adherence of physical activity recommendations comparing overweight/obese and normal-weight adults resulted in significantly lower adherence for the subjects with overweight/obesity [21].

The study aim was to determine the convergence between self-reported adherence and serum 25(OH)D₃ levels. Thereafter, to compare the adherence to D₃ supplementation between children with obesity vs normal-weight children.

Informed consent and written assents were obtained from participants and parents. This study was approved by the Central Ethical Review Board, Sweden Dnr2013/153-31.

Material and Methods

The study design was a prospective longitudinal study of 20 children with a low D₃ status. Inclusion criteria: age 11 -18, Tanner stage ≥ 3, 25(OH)D₃ ≤ 50nmol/L, otherwise healthy Obesity was defined as >2.0 BMI SDS [22].

Procedure

All children were recommended D₃ supplementation calculated by BMI SDS; children with obesity were recommended 2.000 IED3 and normal-weight children were recommended 1.000 IE D3 [23].

The supplementation was vitamin D₃ 1.000 IE/tablet (Ferosan, Sweden) and continued for 2 months. Blood samples were obtained at 3 time points, at baseline and after 4 and 8 weeks. The children were also asked to evaluate their own adherence after 4 and 8 weeks using a Likert scale with 1 representing children who never takes D₃ supplementation (very poor), 2 representing children who sometimes takes D₃ supplementation, 3 representing children who usually takes D₃ supplementation, 4 representing children who regularly takes D₃ supplementation and 5 representing those who always take their supplementation [18]. Score 4 and 5 was defined as high adherence.

Parameters

Anthropometric: weight, height, and BMI standard deviation scores (BMI SDS) were measured at baseline. Biomarkers: 25(OH) D₃ nmol/L, parathyroidhormone (PTH)pmol/L, calciummmol/L, f-glucosemmol/L, f- insulinmIE/l and HbA1c mol/mol were analyzed at baseline and after 1 and 2months.

Statistical analysis

Descriptive data are presented as the median and range.

Parameters were assessed using the Wilcoxon signed rank test for dependent samples, the Mann-Whitney U Test for independent samples and related samples test.

Correlations were assessed using Spearman’s rank order correlation.

Statistical analyses were performed using SPSS for windows version 22 (SPSS, Illinois, USA).

Results

Demographic characteristics of the children studied are summarised in Table 1.



The children were recruited from Rikscentrum Barn Obesitas, Karolinska University Children Hospital in Stockholm and from a primary school in Huddinge, Sweden during November-February 2014.

Twenty-eight children were asked to participate in the study to achieve a number of 20 participants, 12 children with obesity and 8 with normal-weight.

Adherence to the D₃ supplement was followed for 2 months and was documented in combination with blood samples. All the participants had a high self-documented adherence after 1 and 2 months (90%, 75% respectively) with no difference between children with obesity and normal-weight children.

Median 25(OH)D₃ level at baseline was 37 (15-50) nmol/L in all studied children; 24(15-50) nmol for children with obesity versus 40(22-49) nmol/L for normal-weight children (p=0.2) (Table 1).

25(OH)D₃ levels increased significantly after 2 months, (p <0.001), with no difference between children with obesity compared with normal-weight children; 29(16-54) and 21(11-32) nmol/L respectively (p=0.9) (Figure 1).

Ninety % of all children increased their levels of 25(OH)D₃ to > 50nmol/l, which is defined as normal using the IOM definition [11,24].

A significant correlation was found between basic levels of

25(OH)D₃ and the increase of 25(OH)D₃, i.e. a lower 25(OH)D₃ value resulted in a greater increase (r=0.7).

All children who increased their 25(OH)D₃ levels to > 50 nmol/l after 1 month still had increasing 25(OH)D₃ levels during the last month of D₃ supplementation.

No other differences were seen in metabolic risk markers after 2 months, Table 1.

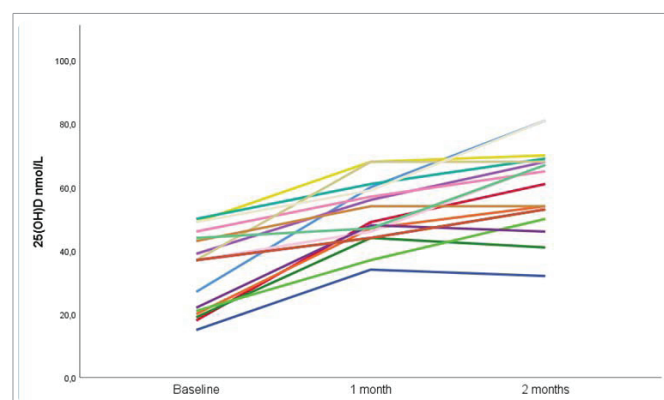


Figure 1: Comparing 25(OH)D₃ levels baseline, 1 and 2 months after recommendation of D₃ supplementation in obese and normal-weighted children.

Table 1: Demographics of the studied children.

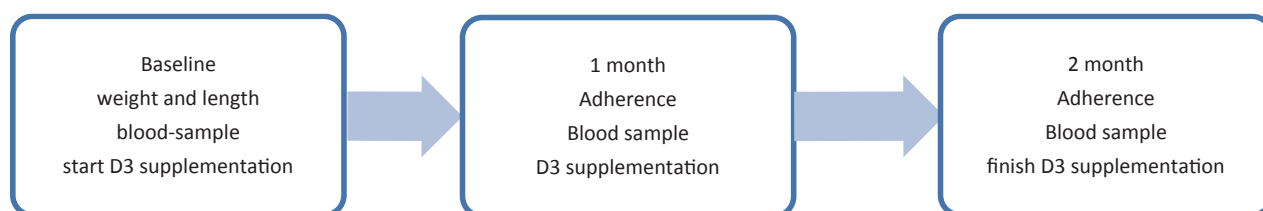
		All children				Children with obesity				Children with normal-weight			
		n=20				n=12				n=8			
Gender male/female		9/11				5/7				4/4			
Age		14.8(11-17.5)				3.4(2.1-4)				0.56(1-1.34-1.84)			
BMI SDS		2.43(-1.34-4)											
25(OH)D3	nmol/l	37 (15-50)	49(34-68)	62(32-81)	<0.001	24(15-50)	48(34-68)	62(32-81)	<0.001	40(22-49)	51(44-68)	60(46-81)	<0.001
25(OH)D3 change	nmol/l			23.5(11-54)				29(16-54)				21(11-32)	
Parathyroid hormone	pmol/l	5.8(2.6-8.6)	4.8(2.7-9.2)	5(2.7-8.9)	0.9	5.2(3.1-7.2)	3.9(2.7-7.4)	4.8(2.7-8.8)		5.9(2.6-8.6)	5.8(4-9.2)	5.4(3.8-8.9)	
Calcium	mmol/l	2.4(2.24-2.49)	2.32(2.17-2.51)	2.35(2.13-2.49)	0.2	2.4(2.33-2.49)	2.34(2.17-2.46)	2.36(2.13-2.49)		2.36(2.24-2.47)	2.31(2.21-2.51)	2.33(2.21-2.45)	
Phosphate	mmol/l	1.3(1-1.8)	1.3(0.9-1.7)	1.2(0.9-1.9)	0.9	1.2(1-1.7)	1.3(1-1.7)	1.2(0.9-1.8)		1.3(1.1-1.8)	1.4(0.9-1.7)	1.4(1.1-1.9)	
Glucose	mmol/l	5.3(4.3-6)	5.2(4.5-6)	5.2(3.8-5.9)	0.6	5.2(4.3-6)	5.1(4.6-6)	5.3(3.8-5.8)		5.3(4.9-5.7)	5.3(4.7-5.9)	5.2(4.9-5.8)	
Insulin	mIE/l	12(6.3-62)	14.5(6-56)	18(5.5-84)	0.5	21(6.3-62)	26.5(7.6-56)	25.5(8.5-84)		11(8.8-12)	8.4(6-16)	8.8(5.5-17)	
HbA1c	mmol/mol	32(23-35)	32(28-36)	32(24-38)	0.3	33.5(23-35)	33(28-36)	32(24-38)		31.5(28-34)	32(30-34)	32(30-34)	

values are given as median and range

* Baseline p=0.2 Mann Whitney U test

** 1 month p=0.3

*** 2 months p=0.9



Flow Chart

Discussion

Our pilot study shows that it is possible to increase a low D₃ status in children with obesity and normal-weight children depending on a high adherence to recommended D₃ supplementation.

Self-reported adherence is a practical way to measure adherence, because of its low cost and can easily be implemented into the clinical work.

There is discussed if adherence to medication/supplementation is affected by multiple barriers, which can be framed by the health-cares hurdles [16]. In the present study adherence was high due to frequent contact with the paediatric nurse, who monitored the intake of supplementation and performed the blood samples. All the participants were interested to follow their 25(OH)D₃ levels, which probably motivated the participants for taking D₃ supplementation. Our result, demonstrates the importance of regular follow-up visit with a health care provider, which is in line with previous studies [25].

We may speculate about how the convergence between self-reported adherence and D₃ status would be without blood-sampling. However, a recent review study presented that self-reported adherence was predictive of clinical outcomes [19].

In this longitudinal study of D₃ insufficient children, we found that 90 % of the children reached a normal D₃ status when children with obesity were recommended 2000 IE D₃ compared with 1000 IE to normal-weighted children. We found no difference in changes of 25(OH)D₃ levels when comparing children with obesity and normal-weight children. Our result may indicate that obese children need a higher D₃ dose compared with normal-weight children. This is in line with a recent published review, presenting the current recommendations for correction of D₃ insufficiency in children with obesity and underlines the need for higher D₃ doses in overweight and obese children [26].

Strengths and limitations of the study

The strength of our study was the opportunity for continued care, including frequent blood sampling as a good direct marker of adherence. Our pilot study also has important limitations as the number of subjects was small, but the results clearly show the importance of regular visits to care providers with a good marker for adherence.

We already know when living in northern latitudes that sunlight in isolation is insufficient to generate an adequate D₃ status [27] and we also know that some groups of children are at high risk of D₃ insufficiency/deficiency, as children with obesity and in dark-skinned children [26,28]. Therefore, future larger intervention and interview studies should be conducted to understand factors that contribute to an improvement of adherence, which saves money and gives health benefits to different group of children.

Conclusion

The convergence between self-reported adherence and serum 25(OH)D₃ levels was high. The adherence to D₃ supplementation was good, due to frequent contacts with a pediatric nurse and blood sampling, measuring 25(OH)D₃, with no difference between obese or normal-weight children.

Acknowledgments

I would like to thank the Sallskapet Barnavard Foundation, the Stiftelsen Samariten Foundation and the Crown Princess Lovisa Foundation.

The author declares that there is no conflict of interest regarding the publication of this paper.

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