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ORIGINAL ARTICLE

Effect of vitamin D supplementation on growth parameters in children with Vitamin D deficiency

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Abstract:
Objectives: To study the effect Vitamin D supplementation on weight and height standard deviation score in Vitamin D deficient children. Material and methods: The study was conducted by selecting Vitamin D deficient children based on serum. Vitamin D level and their Weight and Height was measured. One dose of 3,00,000 IU intramuscular along with calcium (50 mg/kg/day) was given to all the children. After 3 months, serum Vitamin D level, weight and height standard deviation Score was measured and the subjects were randomly divided into two groups. A balanced block randomization method was used to randomize the participants, into Group 1 and 2. The first Group received Calcium (50 mg/kg/day) and the second Group received 400 IU/day of Vitamin D3 along with Calcium (50 mg/kg/day) for 9 months. After 9 months, serum Vitamin D level, Weight Standard Deviation Score and Height Standard Deviation Score was measured. Results: Age of the study subjects in group 1 was 3.5±0.8 years whereas that in group 2 was 3.3±0.7 years. Mean Wtsds in group 1 was 0.42±0.01 whereas that in group 2 was 0.39±0.02. There was a significant positive correlation between serum vitamin D level and Wtsds and Htsds. The increment in Wtsds was much lower in group 1(0.42±0.07) as compared to group 2(1.15±0.01) and this difference was statistically significant. The increment in mean Htsds was 0.07±0.01 in group 1 which was significantly lower than that in group 2 (0.35 ± 0.02). Conclusion: The present study showed that the weight standard deviation score and height standard deviation score progressively improved with the vitamin D supplementation.

Keywords: *Serum Vitamin D levels, weight standard deviation score and height standard deviation score*
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Introduction

Vitamin D deficiency was never suspected in a subtropical country like India till 1990s. People in India are neither excessively light nor dark. However till the year 2000, there was no systematic study which directly assessed Vitamin D level in India. In 2000, for the first time serum 25-hydroxy Vitamin level was measured using a sensitive and specific assay in apparently healthy subjects in Delhi and it was shown that significant hypovitaminosis D was present in 90% of the study subjects (1). A study from North India in villages around Delhi showed that the mean 25(OH)D level in the rural area was 36.4 ± 22.5 nmol/l/L (2). Males had significantly higher 25(OH)D levels than females. The mean 25(OH)D level of rural males and females was six and three times higher than their urban counterparts. Even with five hours of daily sunshine exposure, serum 25(OH)D levels was ≥ 50 nmol/L in only one third of the cases.

In another study from Asia, serum 25(OH)D deficiency (<15 ng/ml) was seen in 66.3% of the

Table 1. Recommended treatment regimens

Group	Daily regimen (8-12 weeks)	Weekly regimen (8-12 weeks)	Stoss therapy (oral or IM)	Maintenance
< 1 month old	1,000 IU	50,000 IU	-	400-1,000 IU
1-12 months old	1,000-5000 IU	50,000 IU	1 lakh -6 lakh units over 1-5 days	400- 1,000 IU
			(Preferably 3 lakh)	
1-18 years old	5,000 IU	50,000 IU	3-6 lakh units over 1-5 days	600-1,000 IU
>18 years old	6,000 IU	50,000 IU	3-6 lakh units over 1-5 days	1,500-2,000 IU

subjects. Severe vitamin D deficiency was found in 20.6% subjects(<5 ng/ml), 27.2% had moderate vitamin D deficiency (5-9.9 ng/ml), while 18.5% had mild vitamin D deficiency (10-14.9 ng/ml). When a serum 25(OH)D level of 20 ng/ml was used as a cut off, 78.3% subjects were diagnosed to be vitamin D deficient (3).

In a study from New Delhi, it was observed that Vitamin D supplementation resulted in increased level of vitamin D at six months by measuring plasma calcidiol levels. Vitamin D therapy resulted in significantly increased standard deviation (z) scores at six months for weight, length, and arm circumference and decreased the proportion of children with stunted growth (length for age z score ≤2) or with arm circumference z scores of 2 or less (4).

Subsequently, a series of studies from different parts of our country have pointed toward widespread Vitamin D deficiency in India, in all age groups. Recent data indicate that Vitamin D deficiency is pandemic and even the healthy and the young are not spared (5).

While there is no consensus on the definition of vitamin D deficiency and sufficiency, the American Academy of Pediatric in their revised guidelines (2008), states that on the basis of the available evidence, serum 25(OH)D concentration in children should be >50 nmol/l Stoss therapy regimens include large oral or parenteral dose of vitamin D3 which has been shown to cause increased and sustained higher levels of 25(OH)D, especially the regimen with 6 lakh IU. Stoss therapy is safe and can lead to hypercalcemia only at very high doses (Table-1). Doses of 1,50,000 to 3,00,000 IU can be effective with less side effects.

There are very few studies which showed the effect of Vitamin D supplementation on growth parameters of children with Vitamin D deficiency. Therefore, we planned this study to observe the effect of vitamin D supplementation on weight and height standard deviation scores in Indian children (20ng/ml).

Material and Methods

To study the effect of Vitamin D on growth parameters in children with Vitamin D deficiency. A prospective randomized controlled trial was conducted in the Department of Pediatrics, GSVM Medical College, L.L.R and associated hospitals, Kanpur.

Selection of cases: All children between 2 to 5 years age group attending pediatrics OPD in GSVM Medical College during the study period presenting with vitamin D deficiency. A total of 132 subjects were included.

Exclusion Criteria:

1. Children with chronic illness.
2. Children on steroid therapy and other factors influencing growth in children.
3. Acute illness of <2 weeks duration.

Table 2. Baseline characteristics of study subjects in the two groups at 3 months

Determinant	Group 1 (n=53)		Group 2 (n=51)		P value
	Mean	SD	Mean	SD	
Age	3.5	0.8	3.3	0.7	>0.05
Serum calcium (meq/l)	4.18	0.35	4.75	0.29	>0.05
Serum phosphorus (meq/l)	4.45	0.16	4.54	0.18	>0.05
Serum Vitamin D levels (ng/ml)	22.35	4.31	23.46	4.21	>0.05
Wtsds	0.42	0.01	0.39	0.02	>0.05
Htsds	0.30	0.02	0.37	0.03	>0.05

The study was conducted by selecting Vitamin D deficient children based on the criteria of serum Vitamin D level <20 ng/ml. Weight Standard Deviation Score and Height Standard Deviation Score was measured in all the vitamin D deficient children. One dose of 3,00,000 IU vitamin D intramuscular along with Calcium (50 mg/kg/day) was given to all the children. After 3 months, serum Vitamin D level, Weight Standard Deviation Score and Height Standard Deviation Score (6,7) was measured and the subjects were randomly divided into two groups. A balanced block randomization method was used to randomize the participants, into Group 1 and 2.

Group 1 received Calcium (50 mg/kg/day) and Group 2 received 400 IU/day of Vitamin D3 for 9 months along with along with Calcium (50 mg/kg/day). After 9 months, serum Vitamin D level, Weight Standard Deviation Score and Height Standard Deviation Score was measured.

Statistical Analysis: Data was compiled using Microsoft Excel and analysed using SPSS 17.0. Quantitative variables were analysed using Mean and Standard Deviation. Comparison between the two groups was done using Student's t test. Pearson's correlation coefficient was used to study the correlation between two quantitative variables. Paired t test was used to analyse the difference between before and after values.Two tailed p value less than 0.05 was considered significant.

Results

At three months, the baseline characteristics of the two groups were comparable (Table 2). Age of the study subjects in group 1 was 3.5±0.8 years whereas that in group 2 was 3.3±0.7 years. Serum calcium of the study subjects in group 1 was 4.18±0.35 meq/l and in group 2 was 4.75 ± 0.29 meq/l. Serum vitamin D level in group 1 was 22.35±4.31 ng/ml whereas that in group 2 was 23.46±4.21 ng/ml. Mean Wtsds in group 1 was 0.42±0.01 and in group 2 was 0.39±0.02 ng/ml.

Table 3. Correlation between serum Vitamin D level and growth parameters at 12 months (n=104)

Variable 1	Variable 2	Correlation coefficient	P
Vitamin D	Wtsds	0.651	0.028
Vitamin D	Htsds	0.623	0.016

Correlation analysis was done between vitamin D level and Wtsds and Htsds for all the study subjects at 12 months (Table 3). There was a significant positive correlation between serum vitamin D level and Wtsds (correlation coefficient = 0.651). The correlation between serum vitamin D level and Htsds was also

Table 4. Increment in Wtsds from 3 months to 12 months in the two groups					
Wtsds	**At 3 months**		**At 12 months**		P
	Mean	**SD**	**Mean**	**SD**	
Group 1 (n=53)	0.42	0.01	0.84	0.01	<0.01
Group 2 (n=51)	0.39	0.02	1.54	0.02	<0.01

statistically significant (correlation coefficient = 0.623)

In group 1, the mean Wtsds increased from 0.42±0.01 to 0.84±0.01 wheareas in group 2, the Wtsds increased from 0.39±0.02 to 1.54±0.02 and this increment was statistically significant and was greater in group 2 where vitamin D supplementation was given in addition to calcium (Table 4).

Table 5. Increment in Htsds from 3 months to 12 months in the two groups					
Htsds	**At 3 months**		**At 12 months**		**P**
	Mean	**SD**	**Mean**	**SD**	
Group 1 (n=53)	0.30	0.02	0.37	0.07	<0.01
Group 2 (n=51)	0.37	0.03	0.72	0.01	<0.01

In group 1, the mean Htsds increased from 0.03±0.02 to 0.37±0.07 wheareas in group 2, the Htsds increased from 0.37±0.03 to 0.72±0.01 This difference was statistically significant and was greater in group 2 where vitamin D supplementation was given in addition to calcium (Table 5).

The increment in mean level of vitamin D was 1.45±0.39 ng/ml in group 1 which was significantly lower than that in group 2 (21.68±5.24 ng/ml) (Table 6). The increment in Wtsds was much lower in group 1(0.42±0.07) as compared to group 2 (1.15±0.01) and this difference was statistically significant. The increment in mean Htsds was 0.07±0.01 in group 1 which was significantly lower than that in group 2 (0.35 ± 0.02).

Discussion

The present study showed that the increment in Wtsds was much lower in group 1(0.42±0.07) as compared to group 2(1.15±0.01) and this difference were statistically significant. This finding shows that the weight standard deviation score progressively improved with the vitamin D supplementation. The increment in mean Htsds was 0.07±0.01 in group 1 which was significantly lower than that in group 2 (0.35 ± 0.02). Thus we found positive response of vitamin D supplementation on height standard deviation score. Similarly, BillooA et al. 2009 (8), showed that the with the one dose of vitamin-D (cholecalciferol), there was appreciable gain of weight and height during follow-up. Similar result was also observed in a study from Karachi that following one injectable dose of vitamin-D (cholecalciferol) therapy, there was appreciable gain of weight and height and raised levels of alkaline phosphatase became normal during follow-up (3). Kalra et al. 2012 (9) showed the beneficial effect of vitamin D supplementation during pregnancy on infant anthropometry. Geeta et al. 2011 (4) concluded that vitamin D supplementation during pregnancy increases maternal 25(OH)D level.
Also vitamin D_3 had a beneficial effect on infant anthropometry and a larger dose also improved cord blood alkaline phosphatase. In their study, subjects were randomised in the second trimester to receive either one oral dose of 1500 µg vitamin D_3 (group 1, n= 48) or two doses of

Table 6. Comparison of increment in Serum Vitamin D level, Weight standard deviation score and Height standard deviation score from 3 month to 12 months in the two groups					
	Group 1 (n=53)		**Group 2 (n=51)**		**P**
	Mean	**SD**	**Mean**	**SD**	
Vit D	16.45	5.39	21.68	5.24	<0.01
Wtsds	0.42	0.07	1.15	0.01	<0.01
Htsds	0.07	0.01	0.35	0.02	<0.01

3000 µg vitamin D_3 each in the second and third trimesters (group 2, n =49). Neonatal Ca and cord blood 25(OH)D did not differ significantly in the three groups. Birth weight, length and head circumference were greater in groups 1 and 2 (3·08 and 3·03 kg, 50·3 and 50·1 cm, 34·5 and 34·4 cm, respectively) as compared to the controls receiving usual care (2·77 kg, 49·4, 33·6 cm; P = 0·0001 for length, head circumference and fontanelle and P = 0·003 for weight). These differences were still evident at 9 months.

WHO says that skin exposure of the arms and face to sunlight for 30 minutes(without sunscreen) can fulfill the daily vitamin D needs. But skin synthesis of vitamin D is influenced negatively by factors that reduce the skin's ability to provide the total needs of the individual: latitude and season, ageing process, skin pigmentation (the presence in the skin of darker pigments that interfere with UV light reaching the appropriate layer of the skin), clothing (completely covering the skin for cultural and religious reasons leaves insufficient skin exposed to sunlight) and sunscreen use (widespread use of sun-blockers reduces skin damage by the sun but also adversely affects vitamin D synthesis). Not all of these problems can be solved in all geographic locations, therefore WHO recommends that individuals not synthesizing vitamin D, should correct their vitamin D levels by consuming the age appropriate amounts of vitamin D (10).

Conclusion

The present study concludes that in children 2 to 5 years of age, the weight standard deviation and height standard deviation scores show marked improvement with vitamin D supplementation.

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