Research brief

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Efficacy and safety of a single monthly dose of cholecalciferol in healthy school children

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Abstract

Objective: This study aimed to evaluate the efficacy and safety of a single monthly dose of cholecalciferol in healthy school children.
Methods: A total of 118 children of class VI of a residential school were selected to receive vitamin D supplementation in the form of oral cholecalciferol 60,000 IU monthly. Serum calcium and 25-hydroxyvitamin D (25OHD) levels were estimated at 0 and 12 months. The proportion of subjects achieving vitamin D sufficiency was assessed.
Results: The mean 25OHD levels increased significantly from 12.04±5.27 ng/mL at baseline to 32.6±7.05 ng/mL after 12 months of supplementation ($p<0.001$). None developed hypercalcemia.
Conclusions: Vitamin D supplementation in the doses of 60,000 IU monthly is a reasonable, safe and cost-effective regimen for children to attain and maintain vitamin D sufficiency.

Keywords: dosage; India; supplementation; vitamin D.

Introduction

Vitamin D is an essential factor for optimal bone health, and may impact other medical disorders including autoimmune, neoplastic, granulomatous, and metabolic disorders (1). Vitamin D deficiency is prevalent in healthy school children in India (2, 3). This has been attributed to inadequate sunlight exposure and low vitamin D intake (4). However, the dose and strategy of vitamin D supplementation in children is a matter of debate and the studies are limited. This study aimed to evaluate the efficacy and safety of a single monthly dose of cholecalciferol 60,000 IU, the equivalent of 2000 IU daily, for 1 year in healthy school children residing in Uttar Pradesh, India.

Methods

This study was carried out in a residential school representing children of lower socioeconomic strata in North India. A total of 118 (61 males) school children (median age 11 years, range 9–12 years) of class VI were selected for vitamin D supplementation. Children with hepatic, renal, or malabsorptive diseases and children on medications known to affect vitamin D metabolism were excluded. Two children had 25OHD levels >30 ng/mL and were excluded. There were three dropouts. None of the children had received any calcium or vitamin D supplementation prior to the study. Informed consents were obtained from all the parents of participants. The study was approved by institutional Ethics Committee and was carried out in accordance with the principles of the Declaration of Helsinki.

After an overnight fast, a baseline blood sample was obtained; serum calcium (ionized and total), hemogram, total proteins, and serum albumin were measured on an automated analyzer (Roche Hitachi 912 Chemistry Analyzer, Boehringer Mannheim, Germany). All children were given dinner at 8–9 pm and blood sample was taken at 8–9 am after ensuring fasting status. Vitamin D (cholecalciferol IP) in the dose of 60,000 IU monthly was given in the form of a powder (D Rise, USV Limited, Mumbai, India) with a cup of warm milk. All the subjects who completed 12 months of study took vitamin D as prescribed and were directly observed by a trained nurse.

Subjects were seen monthly on a pre-selected date for a total of 1 year. Serum 25OHD was measured at baseline and at 12 months using chemiluminescence immunoassay (CLIA) (Liaison, DiaSorin, Stilwater, MN, USA). Vitamin D status was graded as follows: severe deficiency <10 ng/mL (<20 nmol/L), deficiency 10–20 ng/mL (25–50 nmol/L), insufficiency 20–30 ng/mL (50–75 nmol/L), and sufficiency >30 ng/mL (>75 nmol/L) as recommended by Lips (5).

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Statistical analysis

All the continuous variables were expressed in terms of mean (SD). Pre- and post-supplementation variables were analyzed in terms of paired Student's t-test after confirming the normality conditions of the distribution. p-Values<0.05 were considered significant. Statistical Package for Social Sciences (SPSS) version 21.0 (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA) was used for statistical analysis of the data.

Results

At the baseline, 43.5% children had serum 25OHD levels below 10 ng/mL (25 nmol/L), 48.7% children had between 10 and 20 ng/mL (25–50 nmol/L), 6.1% had between 20 and 30 ng/mL (50–75 nmol/L), and only 1.7% had above 30 ng/mL (75 nmol/L). The mean serum 25OHD levels were 8.0 ng/mL (19.9 nmol/L), 13.5 ng/mL (33.7 nmol/L), 23.3 ng/mL (58.2 nmol/L), and 33.8 ng/mL (84.4 nmol/L) in the severe deficiency, deficiency, insufficiency and sufficiency groups, respectively (Table 1).

Vitamin D supplementation in the doses used significantly improved serum 25OHD status, such that 60.9% children had above 30 ng/mL (75 nmol/L), 36.5% children had between 20 and 30 ng/mL (50–75 nmol/L), and only 2.6% had below 20 ng/mL (50 nmol/L) at 12 months. Serum calcium levels also improved significantly after supplementation of vitamin D (Figure 1). No student developed hypercalcemia (Table 2).

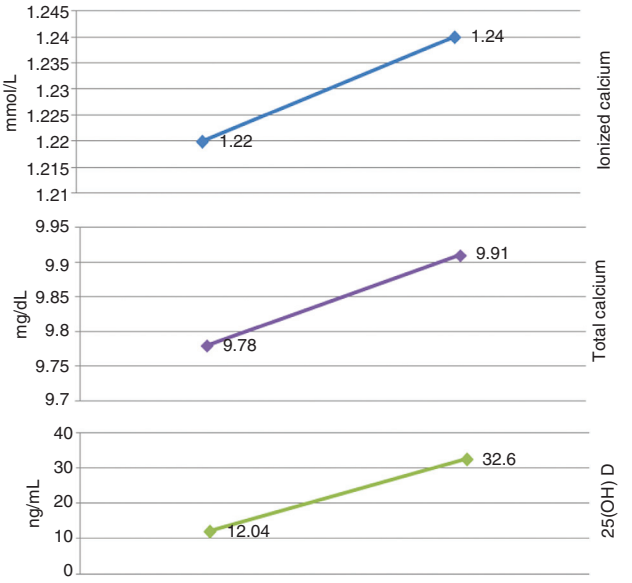

Figure 1: Increments in serum 25OHD, total calcium, and ionized calcium after vitamin D supplementation.

Discussion

In this study, it was proven that oral vitamin D supplementation with a dose equivalent of 2000 IU/day for 1 year safely and significantly increased serum 25OHD levels in all children. Only three (2.6%) children remained vitamin D-deficient at the end of 1 year. However, the mean serum 25OHD levels also improved significantly in these three children.

In a recent study, vitamin D_3 supplementation with 1000 IU daily in children with mean baseline 25OHD concentration <20 ng/mL effectively raised their mean 25OHD concentration to ≥20 ng/mL but failed to reach 30 ng/mL (6). Fuleihan et al. (7) compared 200 IU vs. 2000 IU of vitamin D per day and found that high dose supplementation had better effect on improving the vitamin D status in individuals. Maalouf et al. (7) reported that in children and adolescents with serum 25OHD level below 20 ng/mL (<50 nmol/L), a vitamin D dose equivalent to 2000 IU/day resulted in desirable vitamin D levels. The increment in serum 25OHD levels in response to monthly cholecalciferol supplementation in the present study was similar to that reported by Maalouf et al. (8), using a comparable

Table 1: Vitamin D levels at baseline and after vitamin D supplementation among all participants.

Vitamin D status, ng/mL[a]	Pre-supplementation		Post-supplementation	
	Number %	25OHD Mean±SD	Number %	25OHD Mean±SD
Severe vitamin D deficiency	50 (43.5)	8.0±1.1	0 (0.0)	–
Vitamin D deficiency	56 (48.7)	13.5±2.2	3 (2.6)	17.3±2.8
Vitamin D insufficiency	7 (6.1)	23.3±2.7	42 (36.5)	26.6±2.5

[a]To convert ng/mL into nmol/L, multiply by 2.496.

Table 2: Serum ionized calcium, total calcium, and 25OHD levels before and after supplementation.

Parameter	Pre-supplementation Mean±SD (range)	Post-supplementation Mean±SD (range)	p-Value	95% confidence interval
Ionized calcium, mmol/L	1.22±0.03 (1.14–1.28)	1.24±0.03 (1.14–1.33)	<0.001	−0.02 to −0.01
Total calcium, mg/dL	9.78±0.24 (9.15–10.24)	9.91±0.28 (9.12–10.61)	<0.001	−0.19 to −0.07
25OHD, ng/mL[a]	12.04±5.27 (5.16–27.3)	32.6±7.05 (14.3–51.6)	<0.001	−21.94 to −19.58

[a]To convert ng/mL into nmol/L, multiply by 2.496.

dose of cholecalciferol. In this study, the supplementation of 2000 IU/day did not result in hypercalcaemia or hypervitaminosis D in any subject.

All children had similar dietary calcium intakes (approximately 600 mg/day) and hours of sun exposure (about 60 min/day). Sun exposure was in the form outdoor activity for 60 min/day in the afternoon hours.

Vitamin D supplementation resulted in a significant increase in serum calcium in all children. Other workers also reported improvement in serum calcium levels after vitamin D supplementation (9, 10).

The strengths of our study include relatively long observation period (52 weeks) and the simplicity of monthly dosing schedule. There was 100% drug compliance as cholecalciferol administration was directly observed. Another major strength of our study was the uniformity of study population as they were from class VI of a residential school and had uniform dietary and sun exposure patterns.

The additional advantage of monthly supplementation of vitamin D is its cost-effectiveness. In India, the cost of vitamin D supplementation at 2000 IU/day is INR 1934.0 per annum (30.4 USD) as compared with the equivalent monthly dose of the same brand, which is INR 300.0 per annum (4.7 USD).

However, there were some limitations of our study. First, due to constraints in the study conditions, we could not measure urinary calcium to assess hypercalciuria. However, serum calcium and 25OHD levels were checked post supplementation and hypercalcemia or hypervitaminosis D developed in none. Nonetheless, vitamin D supplementation in doses up to 4000 IU/day over 12 weeks did not result in hypercalciuria (11).

In conclusion, monthly supplementation of cholecalciferol (60,000 IU) may be a reasonable, safe, and cost-effective approach to improve vitamin D status in school children in India.

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Conflict of interest statement

Contributions: MSK, GSJ and AM: design of the study, collection and analysis of data, and writing of the manuscript; SKM: collection and analysis of data; DN: laboratory work
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Competing interests: None

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