EDITORIAL

Do Healthy Pre-pubertal Girls Need Supplementation with Vitamin D?

ANJU SETH

From the Department of Pediatrics, Lady Hardinge Medical College, New Delhi, India.
anjuseth.peds@gmail.com

Vitamin D deficiency and its skeletal consequences are highly prevalent in India. Most of this evidence is from studies conducted on infants, pregnant/lactating women, adolescents, young adults and the elderly, which have documented a prevalence of deficiency ranging between 70 to >90% [1]. Symptomatic vitamin D deficiency also has been predominantly reported in infants/toddlers [2,3] and adolescents [4,5]; not surprisingly, because symptoms of vitamin D deficiency tend to be more frequent in age groups characterized by phases of rapid growth. There is scant information on prevalence of asymptomatic vitamin D deficiency in pre-pubertal age group from India, and even less on symptomatic deficiency. A study from Pune in this age group reported a mean serum 25-hydroxy vitamin D (25(OH)D) level of 24.6 ng/mL with 34.2% prevalence of vitamin D deficiency [6], while a higher prevalence in school children has been reported from Delhi by Marwaha, *et al*. [7]. Limited evidence indicates that the risk of vitamin D deficiency may be lower in this age group as compared to pre-school children [8].

In a study published in the current issue of the Journal, Marwaha, *et al*. [9] have addressed the issue of vitamin D deficiency in pre-pubertal children. They supplemented 216 apparently healthy pre-pubertal girls from Delhi with three different daily oral doses of vitamin D for 6 months. All 300 girls initially meeting the study inclusion criteria had serum 25(OH)D levels <20 ng/mL at baseline. The authors found a dose-dependent increase in serum 25(OH)D level in the participants, with vitamin D sufficiency achieved in >90% girls in all groups. There was a significant increase in serum procollagen type I N-terminal propeptide (PINP), a marker of bone formation. A significant fall was observed in serum carboxy-terminal telopeptide (CTX), a marker of bone resorption, and prevalence of hyperparathyroidism. The urinary calcium creatinine ratio (Ca/Cr) showed a significant increase post-therapy as compared to baseline levels. There was no difference in urinary Ca/Cr, PINP or CTX among the three vitamin D dose groups. There was no comment on incidence of hypercalcemia, hypercalciuria or fall in serum alkaline phosphatase levels with treatment. The authors concluded that while daily supplementation with 600 IU vitamin D, the dose currently being recommended by the Indian Academy of Pediatrics [10], achieved a state of sufficiency in 91% girls, 1000 IU was required to achieve the same in 97% girls.

What are the implications of this study? One assumes that the basic purpose of conducting such study would be to guide pediatricians and policy makers regarding the optimum dose of vitamin D needed for preventive supplementation at the community level. Do we have enough evidence to recommend routine supplementation of healthy pre-pubertal girls with vitamin D, and does this study strengthen this evidence?

First, let us examine the clinical relevance of asymptomatic vitamin D deficiency. Vitamin D deficiency and low bone mineral density (BMD) have been previously reported to coexist during adolescence by the authors of the present study; though, no direct relationship has been demonstrated [11]. A recent study from China found that while more than one-third of the 1582 included children (aged 6-18 years) had vitamin D deficiency, poor BMD was found in less than 2% [12]. There were no significant correlations between serum 25(OH)D concentrations and BMD obtained for total body and at various skeletal sites regardless of whether children evaluated were sufficient, insufficient, or deficient in vitamin D. Similar lack of correlation between vitamin D status and BMD has been reported from a study on pre-pubertal children from Sweden [13] and by the authors of the present study [14]. In the current study too, even though all recruited girls had vitamin D deficiency at enrolment, hyperparathyroidism was present in only 14.8%. It persisted in 4.5% even at follow-up. While there was a significant change in serum markers of bone turnover with supplementation, the clinical implications of this finding are uncertain as

pediatric reference data for these parameters do not exist at present. The levels of PINP and CTX are known to be influenced by food intake, circadian variations, and stage of puberty [15]. BMD was not assessed in the present study. Thus, no clear benefit of 'normalization' of serum vitamin D level is evident either in the existing literature, or from the results of this study.

On the other hand, authors have observed an increase in urinary calcium excretion, an effect that was not different between the three vitamin D dose groups. If vitamin D is to be supplemented to this age group without biochemical monitoring, there is a potential risk of development of hypercalciuria, especially among those recipients who may not be vitamin D deficient to begin with. The risk would increase with increasing duration of supplementation beyond 6 months. However, if supplementation is limited to 6 months as done in the present work, the achieved vitamin D sufficiency is not likely to be sustained beyond one year [16], negating whatever benefits are achieved.

Thus, while the study provides evidence about the optimum dose of vitamin D needed for supplementation in pre-pubertal age group to reach what is currently agreed upon to indicate a state of vitamin D sufficiency, the results should not be interpreted as endorsing universal supplementation in healthy pre-pubertal children. Also, all children included in this work were deficient in vitamin D to begin with. Caution is needed before the results from this study are extrapolated to the community where the prevalence and severity of vitamin D deficiency is not likely to be uniform. Given the facts that (*a*) there is lack of data on prevalence of vitamin D deficiency among healthy pre-pubertal children in India, (*b*) there is no clear evidence of benefits – skeletal or extra-skeletal – of maintaining vitamin D levels >20 ng/mL in this age group, and (*c*) there is risk of hypercalciuria if unmonitored supplementation is continued for a prolonged period, routine supplementation of healthy pre-pubertal girls is not justified in India at present.

Funding: None; *Competing interests*: None stated.

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