

Vitamin D: For Whom and How Much?

We read with interest the recommendations on prevention and treatment of vitamin D and calcium deficiency [1]. While welcoming this article that served the need of the hour, we have the following comments.

Our first observation pertains to risk of vitamin D toxicity likely to be associated with use of bolus doses of vitamin D for treatment of rickets in infants. The authors recommend 60,000 IU vitamin D weekly for 6 weeks as treatment for rickets in all infants >3 months of age. They have quoted Endocrine Society USA guidelines [2] for the same, which in fact recommend a dose of 50,000 IU weekly. This recommendation was based on a single study [3] that was underpowered, with a final sample size less than estimated. Hypervitaminosis was observed in 3/35 infants enrolled in that study. A rapid rise in vitamin D levels with one- or two-monthly bolus doses of vitamin D in infants has also been reported by others [4,5]. Thus, there is no evidence that 60,000 IU vitamin D weekly for 6 weeks is a safe regimen in infancy, while there are definite pointers that this may be associated with serum vitamin D exceeding safety limits, especially since lower doses are known to heal rickets [6]. Moreover, the recommendation of a Tolerable Upper Limit of rather large doses of 1000 to 3000 and 4000 units daily [1], presumably indefinitely, has no supporting literature and may be toxic [7].

Our second observation pertains to preventive supplementation. While there is sufficient Global and Indian literature to recommend universal pharmacological supplementation for all infants not deriving their intake from formula milk, there is a scarcity of studies between 3 and 10 years age. This is an age group where we do not usually encounter nutritional rickets. Thus, recommending vitamin D intake to all children in this age group is not backed by evidence. Adolescents (particularly girls) and pregnant women have been documented to have high prevalence of deficiency in studies from Northern and Central India, and deserve supplementation, but much more data are needed from the Southern and coastal states and the North-East of our country, in all age groups. Universal recommendation of supplementing all children and adolescents, therefore, lacks evidence, apart from being impractical.

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AUTHORS' REPLY

For treatment of rickets, the Guideline for Vitamin D and Calcium in Children' Committee has recommended a dose of 2000 IU/day of vitamin D orally for a minimum duration of 3 months to be followed up with maintenance doses. We have further recommended that larger doses may only be considered when compliance or absorption from gut is an issue, in infants over 3 months of age [1]. Thus, it is not a recommendation for 'all' infants.

The Global Consensus Statement has recommended 2000 IU/day of vitamin D for a period of three months for treatment of rickets. Further, they have advised a 50,000 IU single dose if a bolus dose is to be given. The total dose received, if 2000 IU/day is administered as per their recommendations, comes to 180000 IU in 90 days, while the bolus dose is 50,000 IU [2]. This issue was considered by the Committee when all Guidelines were reviewed and after deliberation, the Committee decided on a weekly dose as advised by the Endocrine Society Clinical Practice Guideline [3]. Further, the Committee also decided on recommending 60,000 rather than 50,000 IU as

a bolus dose as most preparations in the Indian markets contain 60,000 IU.

We agree that there is a limited evidence on dosage for treatment of rickets in infants; thus the Guideline clearly states that it is based on available evidence from Indian studies and other previously published recommendations, which were pertinent to the Indian circumstances. The authors of the query have quoted two studies that reported a rapid rise in vitamin D after 2-monthly bolus doses. The study by Huynh, *et al.* [4] demonstrated the efficacy of bolus dose vitamin D in newborn infants and concluded that bolus dosing of 50000 IU cholecalciferol achieves higher 25 (OH)D (repletion rates) at around 1-2 weeks of age compared to daily dosing, and they report no hypercalcaemia [4]. This study was on newborns (of mothers who had vitamin D concentrations below 75 nmol/L) and the enrolled infants were not diagnosed with rickets. The other study quoted in the query is by Shakiba, *et al.* [5], which is a randomized trial on 120 healthy breastfed infants. They also conclude that a bolus of 50,000 IU of vitamin D every two months with a routine vaccination program provides ideal serum concentrations of vitamin D [5]. They too do not report hypercalcemia, though the study was in infants who were 2.5-4 kg and did not have rickets.

Regarding the second observation, while it is true that rickets does not occur in the age group of 3-10 years, it is also true that bone accrual takes place throughout childhood, and that peak bone mass is built up by second decade. Also, though evidence for extra-skeletal effects of vitamin D is still not compelling, adequate vitamin D status is advisable at all ages [6]. Further, as mentioned,

the guideline is based on the assumption of minimal sun exposure; children and adolescents receiving adequate sunlight exposure or dietary vitamin D do not require supplementation.

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Treat Worm Infestation Before Proceeding Further in Cases of Anemia

We read with interest the recent publication in *Indian Pediatrics* by Narang, *et al.* [1], and have the following comments to offer:

1. Anemia is commonly associated with Celiac disease [2]. This research article would be useful in making the clinician more aware of possibility of celiac disease in cases of unexplained anemia.

2. The subset of excluded patients does not include information about the patients with worm infestation; although, stool examination was performed in the study. It is an important information because a sizable number of children in our country have worm infestation as an important identifiable cause of anemia [3,4]. If worm infestation is detected, it should be treated before proceeding for any further workup. Other conditions, including celiac disease should be suspected if anemia does not respond to anthelmintic and iron therapy.

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