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Letter to Editor

Neonatology Section

Are We Justified in Withholding Routine Vitamin D Supplementation in Trials?

JOGENDER KUMAR[1], ARUSHI YADAV[2]

Dear Editor,

We read with great interest the article by Singh H et al., [1] in the recent issue of your journal. This study reinforces the fact that vitamin D deficiency is pandemic and its supplementation reduces the metabolic bone disease. However, we have a few concerns.

1. Recently published a review of international guidelines on vitamin D deficiency [2] as well as Indian Academy of Paediatrics (IAP) [3] recommends a cut-off of 20 ng/mL as sufficient and <12 ng/mL as deficient. Defining a standard cut-off is very necessary as it greatly affects the prevalence rate of insufficiency/deficiency and hence treatment rate. The cut-offs used in this study (<20 ng/mL as deficient) does not corroborate with recent guidelines. To ensure uniformity, the prevalence of vitamin D deficiency using 12 ng/mL as the cut-off should have been calculated.

2. Vitamin D deficiency is a pandemic and national [3], as well as international guidelines [2], recommend routine vitamin D supplementation. Various studies, including this, have shown the prevalence of vitamin D deficiency in India as high as 60-90%. That's why IAP recommends routine vitamin D supplementation. Recent studies [4] have shown that even 400 IU/day may not be sufficient and higher doses (600-800 IU/day) may be required to prevent deficiency/insufficiency of vitamin D. In this study, the control group was deprived of universal recommendations. It raises a serious issue on the ethical aspect of the study. Furthermore, these babies were monitored with clinical as well as biochemical parameters during follow-up visits. That time the babies in the control group must have been diagnosed to have vitamin D deficiency, still, they were not supplemented. It is unethical to hold treatment/supplementation once we know the results of the investigations and it does not comply with the declaration of Helsinki.

3. It is surprising to note here that at baseline (in control group) babies had preserved vitamin D status despite mothers being deficient. In this study, the baseline and six-month vitamin D and Parathormone (PTH) levels are directly related to each other. It is contrary to the well-known fact that they are inversely related to each other [5]. Both of these findings need to be explained here.

4. The authors mentioned that there was a marked fall in the percentage of the newborn with vitamin D deficiency after six months of vitamin D supplementation and the need for vitamin D in a baby should be individualised. This statement is not supported by evidence. Even their own results contradict it. In the present study despite universal supplementation in the intervention group, 40% were deficient suggesting that 400 IU/day may not be sufficient in preventing vitamin D deficiency. On the other hand, in the control group despite being having normal levels at baseline, 76% became deficient at six months, which warrants universal supplementation and compliance with IAP recommendations [3].

REFERENCES

[1] Singh H, Maria A, Shukla A, Sharma N, Mani K, Das MK. Relation of vitamin d supplementation, upto six months of age with total and bone specific alkaline phosphatase: A randomised control trial. J Clin Diagn Res. 2018;12(10):SC01-SC05.

[2] Randev S, Kumar P, Guglani V. Vitamin D supplementation in childhood - A review of guidelines. Indian J Pediatr. 2018;85(3):194–201.

[3] Khadilkar A, Khadilkar V, Chinnappa J, Rathi N, Khadgawat R, Balasubramanian S, et al. Prevention and treatment of vitamin D and calcium deficiency in children and adolescents: Indian Academy of Pediatrics (IAP) guidelines. Indian Pediatr. 2017;54(7):567-73.

[4] Priyadarshi M, Sankar MJ, Gupta N, Agarwal R, Paul V, Deorari A. Efficacy of daily supplementation of 800 IU vitamin D on vitamin D status at 6 months of age in term healthy Indian infants. J Perinatol. 2018;38(11):1566-72. Available from: http://www.nature.com/articles/s41372-018-0216-6. doi: 10.1038/s41372-018-0216-6.

[5] Sai AJ, Walters RW, Fang X, Gallagher JC. Relationship between vitamin D, parathyroid hormone, and bone health. J Clin Endocrinol Metab. 2011;96(3):E436-46.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Paediatrics, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.
2. Senior Resident, Department of Radiodiagnosis, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Jogender Kumar,
Room No. 3091, Medical College Block, All India Institute of Medical Sciences, Jodhpur-342005, Rajasthan, India.
E-mail: jogendrayadv@gmail.com

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AUTHOR'S REPLY

Query 1 reply: The study was conducted in the time frame where there was a lack of policy for endorsement of vitamin D in Indian infants. Similarly there was no consensus as to define the level of vitamin D to be taken as sufficient or deficient. During the study, as per the available literature, a cut-off of vitamin D below 20 ng/mL was taken as deficient [1,2]. The cut-offs also corroborated with data from United States Institute of Medicine 2011 report, which provides guidelines for cut-off values for routine screening of Vitamin D levels in adults [3]. Indian Academy of Paediatrics guidelines have been instituted to define the Vitamin D deficiency and consensus recommendations in 2017 after completion of our trial [4].

Query 2 reply: The design of the study was such that all the samples were collected at birth but they were analysed at the end of six months. It was only at the end of six months that the actual percentage of vitamin D deficient babies and mothers was calculated by a batch analysis. Till then the samples were stored in deep freezers hence we did not have access to the number of children deficient in vitamin D before six months and none of them showed any features of deficiency clinically. It would not be unethical to deprive the control group from vitamin D supplementation because there was no IAP recommendation regarding supplementation of vitamin D in term neonates in 2013 and there was no routine practice of supplementing babies with vitamin D at the time when the study began, fortunately now we have set guidelines in 2017

[4]. The basic aim of the study was to assess the need of vitamin D supplementation in term babies who were exclusively breast-fed and provide evidence to reinforce this in our Indian population. Even the 2017 IAP guidelines mention the discrepancies in vitamin D deficiency definitions and cut-off levels before the 2017 guidelines were released [4].

Query 3 reply: The finding of preserved vitamin D status in newborns of deficient mothers is an intriguing result as there is ample evidence available to prove that vitamin D status of the mother correlates with that of the baby. But interestingly we did not find the same result. Upon further searches we found another article having similar results [5], thereby challenging the existing notion. The above study would attest to the results that we obtained in our study as 75% mothers had vitamin D status <15 mg/dL and it can be postulated that probably dynamics of vitamin D metabolism changed to improve its absorption and retention in the growing fetus in deficient mothers. The cord blood PTH levels range from 4.8±2.3 pg/mL and accordingly the values corroborate to it. The sample size was inadequate to comment on any relationship between vitamin D and PTH.

Query 4 reply: It is true that 400 IU per day is not sufficient but again the time of the study coincides with the time when no recommendation of vitamin D supplementation in term neonates was being advocated, the (American Academy of Paediatrics) AAP recommendation of 2008 was applicable and according to it, all term healthy breast fed infants need to be supplemented with at least 400 IU per day of vitamin D, hence the choice of dose [6]. This observation could be explained by the fact that vitamin D is required for the growing bones and while the supplemented group could replenish their vitamin D stores, the control group had to face a relative deficiency due to continuous utilization of vitamin D in condition of lack of supplementation and inadequate availability from other sources.

REFERENCES

[1] Goswami R, Gupta R, Goswami D, Marwaha RK, Tandon N, Kochupillai N, et al. Prevalence and significance of low 25 (OH) D concentrations in healthy subjects in Delhi. Am J Clin Nutr. 2000;72:472-75.
[2] Balasubramaniam S. Vitamin D deficiency in breastfed infants and need of routine supplementation. Indian J Med Res. 2011;133(3):250-52.
[3] Ross AC, Manson JE, Abrams SA, Aloia JF, Brannon PM, Clinton SK, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the institute of medicine: What clinician need to know. J Clin Endocrinol Metab. 2011;96(1):53-58.
[4] Khadilkar A, Khadilkar V, Chinnappa J, Rathi N, Khadgawat R, Balasubramanian S, et al. Prevention and treatment of Vitamin D and calcium deficiency in children and adolescents: Indian Academy of Pediatrics (IAP) Guidelines. Indian Pediatr. 2017;54(7):567-73.
[5] Nicolaidou P, hatzistamatiou Z, Papadopoulou A, Kaleyias J, Floropoulou E, Lagona E, et al. Low vitamin D status in mother newborn pairs in Greece. Calcif Tissue Int. 2006;78(6):337-42.
[6] Wagner CL, Greener FR. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008;122(5).

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Arti Maria,
Room no. 239, 2nd Floor, OPD Building, Dr. Ram Manohar Lohia Hospital and Postgraduate Institute of Medical Education and Research, New Delhi-110001, India.
E-mail: artimaria@gmail.com