

Oral Maternal Vitamin D Megadoses to Prevent Vitamin Deficiency in Breastfeeding Mothers and Their Infants

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IT IS ALARMING in the 21st century that women and their breastfeeding infants living in a sun-rich environment could have profound vitamin D deficiency. Also alarming, to date, is the paucity of published clinical studies that seek to present a viable solution to such a critical worldwide public health problem.^{1–9} Thus, the article by Trivedi et al., entitled, “Vitamin D supplementation to mothers during lactation: Effect on 25(OH)D concentration of exclusively breastfed infants at 6 months of age: A randomized double-blind placebo-controlled trial,”¹⁰ should be welcomed as a major contribution in addressing this issue.

Trivedi et al.¹⁰ studied a group of exclusively breastfeeding women of low- to middle-class socioeconomic status living in India, and their response to a vitamin D intervention, dosed to coincide with their term infants’ vaccine/well-child visits. In this clinical trial, 132 women were randomized to receive either a maternal oral dose of 60,000 IU vitamin D₃ versus placebo within 24–48 hours of delivery and then at 6-, 10-, and 14-weeks after delivery for a total of 240,000 IU versus 0 IU vitamin D₃ during this 14-week period. This dose was equivalent to 2,449 IU/day during the 14-week dosing period. The primary outcome was infant total circulating 25(OH)D concentration—the biomarker and indicator of vitamin D status—at 6 months, with secondary outcome markers of bone health—alkaline phosphatase as the biochemical marker and radiographs as the indicator of rickets. Mothers and infants were monitored for clinical signs of hypercalcemia as the marker of vitamin D toxicity during the study period and infants had serum 25(OH)D, calcium and phosphorus, and alkaline phosphatase concentrations measured at 6 months.

Most strikingly, at baseline, in this cohort of women and their infants, virtually all had evidence of what was labeled as insufficiency [25(OH)D <20 ng/mL] and an astounding number (90.4% of mothers and 88.6% of infants) had evidence of profound vitamin D deficiency [25(OH)D level <11 ng/mL]. Cord blood values of 25(OH)D at baseline were critically low: 6.0 and 6.9 ng/mL in the control versus treatment groups. Six infants in the control group and no infants in the treatment group had biochemical evidence of rickets, and there were three infants with radiological evidence of rickets at 6 months—one in the treatment group and two in the control group. Overall, the intervention of oral maternal

supplementation as four bolus doses in the first 14 weeks after birth led to improvement in vitamin D status at 6 months: profound deficiency rates dropped to 5.2% in the treatment group compared with 91.1% of infants in the control group!

Trivedi et al.¹⁰ demonstrated in this study that oral maternal bolus dosing given to coincide with infant vaccinations works to greatly improve infant vitamin D status.¹⁰ The challenge of infant dosing a vitamin supplement in areas of the world where daily intake cannot be assured is well documented. Thus, oral maternal bolus dosing should be considered as a viable public health alternative. Additional study is necessary to clarify if continued bolus dosing of the mother while she is breastfeeding beyond 4–6 months works, to assure continued vitamin D sufficiency in these at-risk infants. As we know, vitamin D’s importance extends beyond the first year of life with anticipated increased requirements during times of rapid growth and during winter months or times of limited sunlight exposure.

The mother herself is at risk for significant deficiency and being vitamin D replete during her child-bearing years is important for her own bone health as well as optimizing pregnancy outcomes should she become pregnant again. Those trials conducted in pregnant women early-on and with the most severe vitamin D deficiency show the most benefit with reduction noted in pre-eclampsia and preterm birth,¹¹ and later, lower risk of allergy and asthma in the offspring.¹²

The findings from this study offer us a glimpse into a problem not seen before with such clarity. Part of the problem lies in the practical implementation of a plan to remedy the situation. The reluctance of the World Health Organization and other international agencies to date to not respond with an all-out public health initiative is tempered by the reality of the limited resources that would have to be directed to fund such an initiative.

Where do we go from here? What can be done by the international community to prevent the degree of deficiency that was demonstrated in this study? The solution it seems is right before our eyes. We can utilize oral maternal vitamin D supplementation to be dosed in a manner sensitive to the social and economic constraints of the community in which each woman lives. In resource-poor countries where the cost of vitamin D may be seen as a burden, alternatives such as judicious sunlight exposure to create endogenous vitamin D in the skin can be considered. Such an approach can only

be implemented in the context of religious and dress customs, and needs to be scientifically documented as a viable alternative.

The bottom line is that this is the time that a comprehensive plan of action must be formulated and rapidly implemented, because, in my mind, as a physician, as a scientist, as a proponent of breastfeeding and healthful behaviors, and lastly, as a mother, one infant with rickets is one infant too many. We must overcome our complacency and act to correct this worldwide most serious public health problem.

References

1. Ala-Houhala M. 25-Hydroxyvitamin D levels during breast-feeding with or without maternal or infantile supplementation of vitamin D. *J Pediatr Gastroenterol Nutr* 1985;4:220–226.
2. Ala-Houhala M, Koskinen T, Terho A, et al. Maternal compared with infant vitamin D supplementation. *Arch Dis Child* 1986;61:1159–1163.
3. Hollis BW, Wagner CL. Vitamin D requirements during lactation: High-dose maternal supplementation as therapy to prevent hypovitaminosis D for both the mother and the nursing infant. *Am J Clin Nutr* 2004;80:1752S–1758S.
4. Wagner CL, Hulsey TC, Fanning D, et al. High-dose vitamin D3 supplementation in a cohort of breastfeeding mothers and their infants: A 6-month follow-up pilot study. *Breastfeed Med* 2006;1:59–70.
5. Oberhelman SS, Meekins ME, Fischer PR, et al. Maternal vitamin D supplementation to improve the vitamin D status of breast-fed infants: A randomized controlled trial. *Mayo Clin proc* 2013;88:1378–1387.
6. Czech-Kowalska J, Latka-Grot J, Bulsiewicz D, et al. Impact of vitamin D supplementation during lactation on vitamin D status and body composition of mother-infant pairs: A MAVID randomized controlled trial. *PLoS One* 2014;9:e107708.
7. Hollis BW, Wagner CL, Howard CR, et al. Maternal versus infant vitamin D supplementation during lactation. A randomized controlled trial. *Pediatrics* 2015;136:625–634.
8. Wall CR, Stewart AW, Camargo CA, Jr., et al. Vitamin D activity of breast milk in women randomly assigned to vitamin D3 supplementation during pregnancy. *Am J Clin Nutr* 2016;103:382–388.
9. Naik P, Faridi MMA, Batra P, et al. Oral supplementation of parturient mothers with vitamin D and its effect on 25OHD status of exclusively breastfed infants at 6 months of age: A double-blind randomized placebo controlled trial. *Breastfeed Med* 2017;12:621–628.
10. Trivedi M, Faridi M, Aggarwal A, et al. Vitamin D supplementation to mothers during lactation: Effect on 25(OH)D concentration of exclusively breastfed infants at 6 months of age: A randomized double blind placebo controlled trial. *Breastfeed Med* 2020. (In press).
11. Rostami M, Ramezani Tehrani F, Simbar M, et al. Effectiveness of prenatal vitamin D deficiency screening and treatment program: A stratified randomized field trial. *J Clin Endocrinol Metab* 2018;103:2936–2948.
12. Wolsk HM, Chawes BL, Litonjua AA, et al. Prenatal vitamin D supplementation reduces risk of asthma/recurrent wheeze in early childhood: A combined analysis of two randomized controlled trials. *PLoS One* 2017;12:e0186657.

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