

Persistent Deficiency for 40% of Toddlers Who Were Vitamin D Deficient as Neonates, Which Cannot Be Assessed by Examining Symptoms of Rickets

Paul Harold George Hogeman¹ Marieke Peternella Hoevenaar-Blom¹ Jos Peter Marie Wielders²

¹Department of Pediatrics, Meander Medical Centre, Amersfoort, The Netherlands

²Department of Clinical Chemistry, Meander Medical Centre, Amersfoort, The Netherlands

Address for correspondence Marieke Peternella Hoevenaar-Blom, PhD, Department of Pediatrics, Meander Medical Centre, P.O. Box 1502, 3800BM Amersfoort, The Netherlands (e-mail: mp.hoevenaar@meandermc.nl).

J Pediatr Biochem 2015;5:12–14.

Abstract

We studied a group of 74 toddlers, mean age 16 months, diagnosed with severe vitamin D deficiency at birth (cord blood <20 nmol/L 25OH vitamin D for neonates). Of 74 initially deficient toddlers, 30 did not reach sufficiency at 50 nmol/L level of serum vitamin D, suggesting persistent vitamin D deficiency over on average 16 months. Boys remained deficient more often than girls. Even in severely deficient toddlers (25OH vitamin D <30 nmol/L), no clinical evidence of symptoms of rickets, growth and development retardation, or abnormal serum calcium levels was observed.

Keywords

- ▶ perinatal
- ▶ vitamin D deficiency
- ▶ rickets
- ▶ toddlers

Introduction

We previously showed a 72% prevalence of vitamin D deficiency in non-Western newborns living in the Netherlands, whereas 24% of West European newborns were deficient (<20 nmol/L 25OH vitamin D in cord blood for neonates, which is comparable to <30 nmol/L for older children).^{1,2}

At the time of the study, the advice of the Dutch Health Counsel was 200 IU (5 μ g) vitamin D₃ daily for exclusively breast-fed infants. Because all formula milk was supplemented with vitamin D, no additional vitamin D supplementation was advised for children exclusively fed by formula milk.³

The objective of our study was to determine whether vitamin D deficiency at birth was normalized at the second year of life and whether there were clinical signs of rickets.

Material and Methods

In a previous study, we observed 164 out of 523 children having perinatal vitamin D deficiency (25OH vitamin D <20 nmol/L in cord blood for neonates) in the Amersfoort region of the Netherlands.¹ From this deficiency group, 74 children

responded to our call for a follow-up visit in early spring 2006 at the age of 12 to 21 months (mean, 15.8 months).

Serum 25OH vitamin D concentration was measured in duplo with the RIA method of DiaSorin (Stillwater, Minnesota, United States). We used the average of the two measurements in our analyses. A blood level of less than 50 nmol/L 25OH vitamin D was regarded as deficient for toddlers.^{4–6} Calcium concentration was measured with an ion-selective assay on a Beckman Coulter analyzer (Unicel Dx C880i analyzer, Beckman Coulter, Brea, California, United States). Breast-feeding and vitamin D supplementation were assessed by questionnaire, and the medical history about growth (related to birth weight) and initiating standing and walking were assessed by a trained physician. Also, the trained physician performed a specific examination⁷ for rickets, including examination for growth retardation, rickets rosary, pigeon chest, craniotables, caput quadratum, epiphyseal swelling, bowed legs, and abnormality of walking.

Statistical analyses were performed with the SPSS statistical software package. This study was approved by the local medical ethical committee.

Results

Of 74 children included, 38 were of West-European (mainly Dutch) and 36 of non-Western origin (mainly Turkish or Moroccan). As an infant, 76% of the toddlers were breast-fed of whom 26% did not receive a vitamin D supplement. As toddlers, 68% received a vitamin D supplement. However, vitamin D supplementation and breast-feeding were not significantly different between children with or without persistent vitamin D deficiency. Median serum 25OH vitamin D level was 53 nmol/L (range: <12 nmol/L–136 nmol/L). Thirty of the 74 children (41%) remained vitamin D deficient (25OH vitamin D <50 nmol/L for toddlers). Eight children (9%) remained severely deficient (25OH vitamin D <30 nmol/L for toddlers). Boys remained deficient more often than girls (► Fig. 1). There was no significant difference in the prevalence of persistent vitamin D deficiency between children of West-European origin (mainly Dutch) or those of non-Western origin (► Fig. 2). Serum calcium levels were within normal ranges (2.20–2.70 mmol/L) for all children except for one toddler with a level of 2.75 mmol/L. This child had a 25OH vitamin D level of 110 nmol/L.

None of the (severely) deficient children showed any clinical sign of rickets. Growth was normal (within normal variations related to birth weight) and no delay in age of initiating standing or walking was reported.

Discussion and Conclusion

Although general practitioners (GPs) were reported of the neonatal vitamin D deficiency, not enough was done for 41% of 74 initially deficient toddlers to reach a 50-nmol/L level of serum vitamin D. The parents of 21 out of the 30 persistent deficient children reported giving them vitamin D supplements. This implies that the supplementation advice of the government of 200 IU (5 µg) vitamin D₃ per day at the time was not enough to correct this deficiency for these children. Boys and children of non-Western origin may be overrepresented in our study compared with all invited children (those with neonatal deficiency in the previous study¹). In our population, 57% were boys and 49% were of non-Western origin, compared with respec-

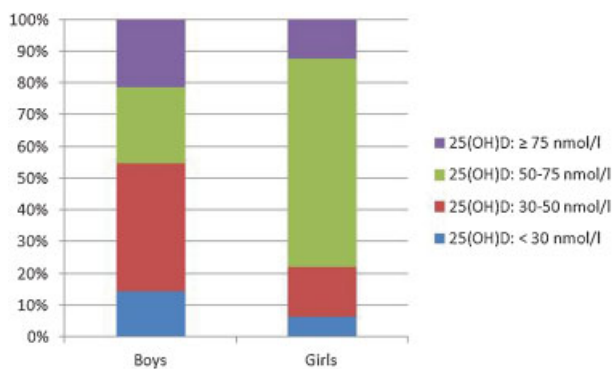


Fig. 1 25OH vitamin D status in 42 boys and 32 girls at age 12–21 months (mean age: 16 months), who were severely vitamin D deficient at birth.

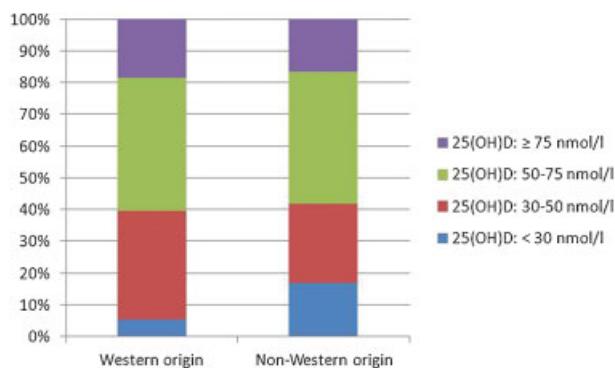


Fig. 2 25OH vitamin D status in 38 children of West-European origin and 36 children of non-Western origin at age 12–21 months (mean age: 16 months), who were severely vitamin D deficient at birth.

tively 50% and 39% of all children who were invited. Because there was no difference in vitamin D status by origin, this will not have influenced our results. However, because boys remain more often deficient in this study, slight overrepresentation of this group may have resulted in slightly higher deficiency rates. The fact that boys remained deficient more often than girls should be replicated in future studies before any conclusions can be drawn. Even at 25OH vitamin D concentrations of less than 30 nmol/L, we observed no clinically evident symptoms of rickets and serum calcium levels were within normal ranges. However, this does not imply that subclinical vitamin D deficiency, measured by serum phosphorus, alkaline phosphates, and PTH levels, does not exist in these children. Vitamin D deficiency should not be taken lightly given the accumulating evidence about early vitamin D deficiency and possible adverse effects later in life: increased risk of developing autoimmune diseases such as diabetes mellitus type 1, multiple sclerosis, rheumatoid arthritis, and an increased risk of osteoporosis and some forms of cancer.⁸ We showed that detecting (moderate) vitamin D deficiency needs measurement of the vitamin D blood level. Hence, even in the absence of clinical signs, health care workers should be aware of the risk of vitamin D deficiency as it is highly prevalent and has the long-term effects.

Acknowledgment

We thank Mrs. N. C. Ran for her support in this study.

References

- Wielders JPM, van Dormael PD, Eskes PF, Duk MJ. Severe vitamin-D deficiency in more than half of the immigrant pregnant women of non-Western origin and their newborns [in Dutch]. *Ned Tijdschr Geneesk* 2006;150(9):495–499
- Wagner CL, Greer FR. American Academy of Pediatrics Section on Breastfeeding; American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics* 2008;122(5):1142–1152

- 3 de Minister van Volksgezondheid, Welzijn en Sport, de Staatssecretaris van Landbouw, Natuurbeheer en Visserij. Voedingsnormen Calcium, Vitamine D, Thiamine, Riboflavine, Niacine, Pantotheenzuur en Biotine. The Hague, The Netherlands: Health Council of the Netherlands; 2000; publication no. 2000/12. Available online at: <http://www.gezondheidsraad.nl/sites/default/files/00@12Nr2.pdf>
- 4 Braegger C, Campoy C, Colomb V, et al; ESPGHAN Committee on Nutrition. Vitamin D in the healthy European paediatric population. *J Pediatr Gastroenterol Nutr* 2013;56(6):692–701
- 5 Gordon CM, Feldman HA, Sinclair L, et al. Prevalence of vitamin D deficiency among healthy infants and toddlers. *Arch Pediatr Adolesc Med* 2008;162(6):505–512
- 6 Ross AC, Manson JE, Abrams SA, et al. The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. *J Clin Endocrinol Metab* 2011;96(1):53–58
- 7 Wharton B, Bishop N. Rickets. *Lancet* 2003;362(9393):1389–1400
- 8 Holick MF. Resurrection of vitamin D deficiency and rickets. *J Clin Invest* 2006;116(8):2062–2072