Vitamin D supplementation could reduce risk of sepsis in infants

Letter to the Editor

A recent paper in this journal identified sepsis syndrome as an important postoperative risk factor for infants below the age of six months and stated that adequate prevention and therapeutic strategies warrant further prospective investigations.[1] Sepsis is caused by bacterial infection. The hormonal metabolite of vitamin D, 1,25-dihydroxyvitamin D, induces production of human cathelicidin, LL-37, which has antimicrobial and antiendotoxin effects that contribute to innate immune response to sepsis.[2] Based on a review of the epidemiology of sepsis in the United States (high rates in winter, low rates in summer, high rates in the northeast, low rates in the west,[3] higher rates for African-Americans than white Americans, and comorbid diseases linked to low serum 25-hydroxyvitmin D [25(OH)D]), it was hypothesized that higher serum 25(OH)D levels could reduce the risk of sepsis.[4] That hypothesis was quickly supported in a study of those with sepsis in an intensive care unit of a hospital in Atlanta, Georgia, finding that those in the intensive care unit with or without sepsis had much lower serum 25(OH)D levels than others in the community.[5] Thus, it would be worthwhile supplementing infants preparing for surgery with vitamin D to bring their serum 25(OH)D levels above 40 ng/mL (100 nmol/L), the level that has generally been found associated with optimal health. Vitamin D3 (cholecalciferol) would probably be more effective than vitamin D2 (ergocalciferol).

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William B. Grant, Ph.D.
Sunlight, Nutrition, and Health Research Center (SUNARC)
P.O. Box 641603
San Francisco, CA 94164-1603, USA
Email: wbgrant@infionline.net
Tel: 1-415-409-1980

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Author reply

We read this letter with much interest and thank the editor for giving us the chance to make some comments. As the design of the reported study[1] was observational and retrospective, conclusions on preventive strategies can only be drawn with caution. According to our results, lower postnatal age and major surgical interventions (e.g., laparotomy with incision of the intestines, or long duration of surgery) are important risk factors for postoperative sepsis syndrome in infants below six months of age. In particular, it was not an aim of our study to investigate the role of vitamin D in postoperative sepsis. We can thus only speculate whether vitamin D supplementation has a potential for prevention of postoperative sepsis. According to a Swiss recommendation in 1998,[2] which is in line with the current recommendation of the Lawson Wilkins Pediatric Endocrine Society in 2008,[3] all patients included in our investigation had received 400 IU vitamin D daily since the fifth day of life. It is a current practice in our institution to supplement preterm infants with even larger doses, usually 600-800 IU daily.[3] Nonetheless, we cannot exclude that some infants might have suffered from hypovitaminosis D in our patient cohort.

Since newborn vitamin D levels strongly rely on maternal vitamin D status,[4] some infants operated on before day 5 and thus not yet supplemented, may have been vitamin D deficient. Furthermore, parental compliance to the recommended vitamin D substitution after discharge is unknown. In addition, hypovitaminosis D may complicate general

undernutrition, in particular in patients in developing countries and the impact of vitamin D deficiency under these circumstances may be much more pronounced. Precise appraisal of vitamin D status in pregnant women is difficult, and not part of current obstetrical practice.[5]

We agree that more research is warranted to elucidate the etiology of postoperative sepsis, possible risk factors and thus also prevention strategies. Considering that vitamin D is a powerful inductor of antimicrobial peptide cathelicidin, which may play an important role in innate host defense, we also agree that vitamin D is a promising substance to promote sepsis prevention in hospitalized patients.[6] However, there is an important lack of knowledge firstly on pediatric patients, secondly on the alterations of the vitamin D metabolism during critical illness, and thirdly on the role of vitamin D in perioperative complications. Furthermore, in neonates and infants the definition of normal ranges for vitamin D levels is still being debated. According to Zeghoud et al[7] neonatal 25-OHD concentrations <30 nmol/L (12 ng/ml) might signify an adequate cut-off for hypovitaminosis D in newborns since these values correlated with increasing parathyroid hormone. Specifically, the causal relationship between low vitamin D levels and infectious complications in children has not yet been investigated *in vivo*.

In conclusion, our study does not allow us to draw conclusions on current recommendations of vitamin D supplementation. However further research on the involvement of vitamin D in perioperative complications, especially in small infants, is needed.

Ulf Kessler, Zacchariou Zacchariou, Luregn J Schlapbach, Steffen Berger
Department of Pediatric Surgery (UK, ZZ, SB)
Department of Pediatrics (LS)
Inselspital, Bern University Hospital and University of Bern, 3010 Bern, Switzerland
Email: Ulf.Kessler@insel.ch

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