Short reports

Plasma 25-hydroxyvitamin D concentrations in preterm infants receiving oral vitamin D supplements

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SUMMARY Plasma 25-hydroxy-cholecalciferol (25-OHD) was measured serially in two groups of preterm infants receiving either 400 IU or 1000 IU oral vitamin D₃ daily. All the babies were able to absorb and hydroxylate vitamin D₃ adequately by 36 weeks' gestational age. The higher daily supplement had no advantage over the lower dose.

Although there are guidelines for daily vitamin D supplementation in term infants,¹ the requirements for preterm infants have not been agreed, and doses of 400,² 800,³ and 1000 IU⁴ have been recommended. The ability of a preterm baby to absorb or 25-hydroxylate vitamin D is disputed. Hillman and Haddad⁵ found no increase in plasma 25-hydroxyvitamin D (25-OHD) levels with oral vitamin D₃ supplements until after 36 weeks' gestational age, whereas Wolf *et al.*⁶ reported an increase in plasma 25-OHD in response to oral vitamin D₃ at 32-34 weeks. We report plasma 25-OHD levels in 18 preterm babies receiving supplements of either 400 or 1000 IU of vitamin D₃ daily.

Patients, methods, and results

18 babies (13 white and 5 West Indian) were randomly allocated to two groups (1 or 2) between July 1977 and February 1978. The birthweights and gestational ages in group 1 and group 2 were 1420 ± 67 and 1562 ± 98 g, and 31.3 ± 0.5 and 30.1 ± 0.5 weeks respectively (mean $\pm$ SEM). The babies were fed with Cow and Gate Premium, breast milk, or both. Those in group 1 received 400 and those in group 2 1000 IU of vitamin D₃ daily by mouth from day 15. Venous blood was obtained with informed parental consent on day 14 after birth and at 36 and 39 weeks postmenstrual age. The left wrist was x-rayed at 36 weeks. Plasma 25-OHD levels were measured by a competitive protein-binding assay, plasma

albumin by the bromocresol green dye binding method, plasma calcium by ethylene glycol tetra-acetic acid titration, and alkaline phosphatase by para-nitrophenyl phosphate hydrolysis. Plasma calcium was corrected for plasma albumin.

The mean plasma 25-OHD concentration at day 14 was 22.7 ± 5.6 in group 1 and 22.0 ± 2.6 nmol/l in group 2 (normal adult range 12.5-100). At 36 weeks plasma 25-OHD levels were significantly higher in both groups (Fig. 1), and the mean level achieved in

Conversion: SI to traditional units—25-hydroxy-cholecalciferol 1 nmol/l $\approx$ 40 ng/100 ml.

Fig. 1 Plasma 25-OHD response to two daily dose regimens of vitamin D₃.

group 2 (45.2 ± 4.7) was higher than that in group 1 (35.0 ± 3.8 nmol/l; $P = \text{NS}$). There was a significant correlation between the plasma 25-OHD level at day 14 and the percentage rise at 36 weeks ($r = -0.68$, $P < 0.0025$) (Fig. 2). Plasma 25-OHD levels measured at 39 weeks were similar to those found at 36 weeks (38.9 ± 5.1 in group 1 and 37.6 ± 2.7 nmol/l in group 2). No significant changes in plasma calcium or alkaline phosphatase occurred during vitamin D supplementation; plasma calcium at 14 days was normal in all but one infant, who was hypocalcaemic (1.74 mmol/l; 7.0 mg/100 ml), and all alkaline phosphatase levels were normal. No infant showed radiological evidence of rickets.

Comment

We have shown that oral supplementation with 400 or 1000 IU of vitamin D3 daily produces a significant rise in plasma 25-OHD levels by 36 weeks in preterm babies without biochemical or radiological evidence of rickets. Although we did not study an unsupplemented group, the lack of change in plasma 25-OHD levels reported by Wolf *et al.*,⁶ and by Hillman and Haddad⁵ in unsupplemented preterm babies, and our finding of higher plasma 25-OHD levels in group 2 indicate that the increase in plasma 25-OHD levels was related to vitamin D supplementation. The negative correlation between the final plasma 25-OHD and the pretreatment level indicates that there

may be constraints on 25-hydroxylation in the pre-term infant, a suggestion which has already been made with regard to adults requiring large vitamin D supplements.⁷ Although higher plasma 25-OHD concentrations were found at 36 weeks in group 2, the higher daily dose does not appear to have any advantages over the more conventional dose of 400 IU.

Our results show that preterm babies can absorb and 25-hydroxylate vitamin D3, but they do not exclude the possibility of either impaired 1α -hydroxylation of 25-OHD⁸ or lack of end-organ response to 1,25-dihydroxyvitamin D3,⁹ either of which could cause rickets in the presence of a normal plasma 25-OHD concentration. In addition, calcium and phosphorus deficiency may sometimes be important aetiological factors.¹⁰ We conclude that daily oral supplements of 400 IU of vitamin D3 are sufficient to produce normal plasma 25-OHD concentrations by 36 weeks in preterm babies.

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Fig. 2 Plasma 25-OHD response to supplementation related to initial level of plasma 25-OHD.