Vitamin D: role in pregnancy and early childhood

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DOI: https://doi.org/10.1159/000332069

Annals of Nutrition & Metabolism

Ann Nutr Metab 2011;59:17–21
DOI: 10.1159/000332069

Published online: November 25, 2011

Vitamin D – Role in Pregnancy and Early Childhood

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Key Words
Vitamin D · Pregnancy · Supplement · Recommendation · Infancy · Recommended intake

Abstract
Several studies in pregnant women and early childhood suggest that vitamin D deficiency (serum 25-hydroxyvitamin D levels <50 nmol/l) is common in both population groups. Recent recommendations have therefore reviewed the literature regarding the role of vitamin D in pregnant women and in early childhood. The Institute of Medicine, in their most recent assessment in 2010, recommended 600 IU per day in pregnant and lactating women. In 2011, the US Endocrine Task Force on Vitamin D commented that 600 IU per day may not be sufficient to correct vitamin D deficiency in pregnant and lactating women. Their recommendation was 1,500–2,000 IU vitamin D per day in pregnant and lactating women with vitamin D deficiency. For infants, the recommendation from both societies is consistently 400 IU vitamin D per day, and also in children both societies recommend 600 IU vitamin D per day. This review will summarize the scientific basis that led to the most recent recommendations.

Threshold Definition for Vitamin D Deficiency and Adequacy

As a general guideline, vitamin D deficiency has been defined as a 25-hydroxyvitamin D level [25(OH)D] of less than 50 nmol/l (<20 ng/ml) in all age groups [1]. At levels below 50 nmol/l, bone resorption and increased PTH levels have been documented [2]. Levels lower than 25 nmol/l (<10 ng/ml) are considered to indicate severe deficiency and can induce adverse effects such as rickets in infants and osteomalacia in adults [2]. Vitamin D adequacy needs to be established in children and pregnant women; however, observational data in younger (age 19–49 years), middle-aged (age 50–64 years), and senior adults (age ≥65 years) suggest that a level of no less than 75 nmol/l is needed for optimal hip bone density [3], and this threshold is consistent with fracture prevention data from double-blind randomized trials in senior adults [4].

Prevalence of Vitamin D Deficiency in Pregnant Women

Surveys of pregnant women in Greece [5], Belgium [6], and the Netherlands [7] suggest that 10–30% of pregnant women have 25(OH)D levels below 30 nmol/l.

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While the threshold of 50 nmol/l was not assessed in the available European studies, the Belgium study documented that 86–88 % of pregnant women did not reach 25(OH)D levels of at least 75 nmol/l [6]. Furthermore, in the Dutch study, 59–84% of pregnant women of non-Western ethnicity had 25(OH)D levels below 30 nmol/l [7]. This high prevalence among pregnant women of non-Western ethnicity may be explained either by a darker skin tone (natural sun protection) or the avoidance of direct sunshine exposure for cultural reasons [8]. The Greek study also measured 25(OH)D levels in newborns and found that their levels were strongly correlated with those of their mothers (correlation coefficient = 0.64), suggesting that the mother's vitamin D status is important for the vitamin D status of the newborn [5]. The high prevalence of vitamin D deficiency among pregnant women led the US Endocrine Task Force on Vitamin D to recommend 25(OH)D assessment in all pregnant women [9].

Prevalence of Vitamin D Deficiency in Early Childhood

During lactation, the newborn largely depends on nutritional sources of vitamin D through breast milk, fortified newborn nutrition, or supplements. To satisfy the requirements of an infant who is only fed breast milk, the mother requires 2,000–4,000 IU per day to transfer enough vitamin D into her milk [10]. Alternatively, as recommended in most countries, newborns should receive a supplement of 400–500 IU vitamin D per day. In a larger survey of German children age 1–17 years, median 25(OH)D levels were 44 nmol/l among native children and 35 nmol/l among immigrant children. The levels of boys and girls were similar; however, there was some decline with age, with the highest median levels measured in the first year of life, likely due to the German supplementation recommendation of 500 IU per day in infants (KiGGS [11]). The Optiford study of 4 Northern European countries (Denmark, Finland, Poland, and Ireland) included 199 children with a mean age of 12.5 years who had serum 25(OH)D levels below 25 nmol/l in 30–50% of cases and serum levels below 48 nmol/l in over 90% of cases [12]. The same study also assessed 25(OH)D levels in seniors and suggested that vitamin D deficiency was more prevalent in children [12].

Why Is It Important to Avoid Vitamin D Deficiency in Pregnant Women? – Relevance for Mother and Child

Relevance for Mothers

Vitamin D deficiency during pregnancy has been associated with an increased risk of preeclampsia [13], gestational diabetes [14], and caesarian section [5], but data from intervention studies are missing.

Relevance for Children

Observational data suggest that increased vitamin D exposure of the mother during pregnancy correlates with better bone health in the offspring. In a longitudinal study of 198 children in the UK, reduced 25(OH)D levels in their mothers during late pregnancy was associated with reduced whole-body ($r = 0.21$, $p = 0.009$) and lumbar spine ($r = 0.17$, $p = 0.03$) bone mineral content in children at age 9 years [15]. This may in part be explained by some data from observational studies [16–19] and small clinical trials [20, 21] suggesting that a higher vitamin D status among pregnant women correlates positively with the birth weight of their offspring, although some observational studies showed a neutral association [22–26]. In a small double-blind randomized controlled trial among 126 Asian women living in London, supplementation with 1,000 IU vitamin D_2 per day compared to placebo in the last trimester of pregnancy led to a greater weight gain in the mothers and reduced the risk of small-for-gestational-age babies (15 vs. 29%) [20]. These findings were supported by another study in Indian women and their offspring comparing a bolus supplementation with 600,000 IU vitamin D in gestational months 7 and 8 and 1,200 IU vitamin D per day in the third trimester to placebo, resulting in significantly higher birth weights with supplementation (bolus vitamin D = 3,180 g; daily vitamin D = 2,890 g; placebo = 2,730 g) [21]. No difference in birth weight was found in a smaller open-design trial comparing two treatment regimens with vitamin D to placebo (200,000 IU once during pregnancy or 1,000 IU per day during the last 3 months of pregnancy) [27]. The largest double-blind randomized controlled trial among 494 Caucasian, Hispanic, and African American pregnant women living in South Carolina by Hollis et al. [28] compared 400 IU to 2,000 IU and to 4,000 IU vitamin D per day. The mean 25(OH)D levels at baseline were about 60 nmol/l, and there was a significant increase in the mean 25(OH)D levels with treatment in all groups at 1 month prior to delivery (400 IU = 81.2 nmol/l; 2,000 IU = 102.6 nmol/l; 4,000 IU = 114.2 nmol/l). With respect to clinical end

points, no adverse events occurred with any of the tested doses, and small but nonsignificant differences in birth weight (400 IU = 3,222 g; 2,000 IU = 3,360 g; 4,000 IU = 3,285 g) and gestational age at birth (400 IU = 38.6 weeks; 2,000 IU = 38.8 weeks; 4,000 IU = 39.1 week) were documented [28].

There is also observational data suggesting that children exposed to more vitamin D during pregnancy may have a lower risk of developing asthma in early life as suggested by two longitudinal studies [29, 30]. Litonjua et al. [31] estimated from two birth cohort studies that the population attributable risk of asthma incidence caused by vitamin D deficiency in pregnancy is about 40% of all cases in children 3–5 years old. In contrast, one study suggested an increased risk of eczema on examination at 9 months (OR 3.26; 95% CI 1.15–9.29) and of asthma at age 9 years (OR 5.40; 95% CI 1.09–26.65) observed in a smaller cohort study among children of mothers who had 25(OH)D levels ≥75 nmol/l compared to children whose mothers had a concentration <30 nmol/l during pregnancy [24]. The study has been criticized for its large loss to follow-up (62%) [24].

Why Is It Important to Avoid Vitamin D Deficiency in Early Childhood?

Bone Health

Rickets is a result of severe vitamin D deficiency and has a significant impact on growth and bone development [32, 33]. While supplementation with 100, 200, or 400 IU per day of vitamin D resulted in the prevention of rickets in one study [34], vitamin D intakes between 340 and 600 IU per day have been reported to have the maximum effect on the linear growth of infants [35]. Furthermore, adding to the concept that vitamin D supplementation in children may not only prevent rickets but also contribute to bone growth and the achievement of an optimal peak bone mass, a 2011 meta-analysis of 4 double-blind randomized controlled trials of vitamin D supplementation in the range of 132–2,000 IU vitamin D per day compared to controls (placebo or lower dose) among a total of 639 children suggested a trend toward a small effect on lumbar spine bone mineral density in all treated children (standardized mean difference 0.15; 95% CI –0.01 to 0.31; p = 0.07). There was also a significant benefit of vitamin D supplementation in children with serum 25(OH)D levels below 35 nmol/l [36], with effects on the total body bone mineral content and lumbar spine bone mineral density equivalent to a 2.6 and 1.7% percentage point greater change from baseline in the supplemented group [36]. Notably, based on one randomized trial among Lebanese girls age 10–17 years included in this most recent meta-analysis, hip bone density increased more with 14,000 IU vitamin D per week (2,000 IU per day) compared to 1,400 IU per week (200 IU per day) at the 12-month follow-up without any report of toxicity and irrespective of baseline 25(OH)D levels [37].

Nonskeletal End Points

In the randomized trial among Lebanese girls comparing 14,000 IU vitamin D per week (2,000 IU per day) with 1,400 IU per week (200 IU per day), there was also a benefit on muscle mass measured by DEXA at the 12-month follow-up [37]. Regarding other nonskeletal benefits of vitamin D in children, observational data support an inverse relationship between a higher 25(OH)D status or vitamin D supplementation and a lower incidence of diabetes [38, 39], atopic allergies [40, 41], and upper respiratory infections [42]. However, evidence from clinical trials in children is very limited. One Finnish birth cohort study suggested that, in infants who received ≥2,000 IU per day of vitamin D compared to no supplementation during the first year of life, there was an 86% reduction in the risk of developing type 1 diabetes in the following 31 years [43]. A recent meta-analysis of four case-control studies of about 6,500 infants found that supplemental vitamin D reduces the risk of type 1 diabetes [OR 0.71 (0.60–0.84)], with higher cumulative doses conferring a greater benefit [44]. Regarding infections, one double-blind randomized controlled clinical trial in 334 Japanese children who received 1,200 IU vitamin D per day compared to placebo documented a 42% reduction in influenza A [45]. A secondary analysis documented an 83% reduction is asthma attacks among children with asthma enrolled in the same trial [45].

Recommendations

The Institute of Medicine, in their most recent assessment in 2010, recommended 600 IU per day in pregnant and lactating women [1]. In 2011, the US Endocrine Task Force on Vitamin D commented that 600 IU per day may not be sufficient to correct vitamin D deficiency in pregnant and lactating women [9]. Their recommendation is

1,500–2,000 IU vitamin D per day in pregnant and lactating women with vitamin D deficiency [9]. For infants, the recommendation of both societies is consistently 400 IU vitamin D per day, and also in children both societies recommend 600 IU vitamin D per day.

Disclosure Statement

The author has nothing to disclose.

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