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Vitamin D supplements during gestation and wheezing in childhood: we need more evidence

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English key words: asthma, wheezing, vitamin D, pregnancy.
Palabras clave en español: asma, sibilancias, vitamina D, gestación.

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Vitamin D supplements during gestation and wheezing in childhood: we need more evidence

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Abstract

Authors' conclusions: growing evidence supports a preventive role of vitamin D during pregnancy on offspring wheeze and/or respiratory tract infections.

Reviewers' commentary: further studies are required to confirm the efficacy and safety of high-dose vitamin D supplementation in pregnancy, since the available evidence is imprecise and there are doubts about its applicability in clinical practice.

Key words: asthma, wheezing, vitamin D, pregnancy.

Suplementos de vitamina D en la gestación y sibilancias en la infancia: necesitamos más pruebas

Resumen

Conclusiones de los autores del estudio: hay una evidencia creciente que apoya un papel preventivo de la vitamina D durante el embarazo y la presencia de sibilancias o infecciones respiratorias de la descendencia.

Comentario de los revisores: se requieren más estudios que confirmen la eficacia y seguridad de las pautas de suplementación a dosis altas de vitamina D en la gestación, ya que la evidencia disponible es imprecisa y hay dudas sobre su aplicabilidad en la práctica clínica.

Palabras clave: asma, sibilancias, vitamina D, gestación.

STRUCTURED ABSTRACT

Objective: to assess the effect of vitamin D (VD) supplementation during pregnancy on wheezing or respiratory tract infection in the offspring in the first 5 years of life.

Design: systematic review and meta-analysis of clinical trials and observational studies.

Data sources: the authors conducted a systematic search of PubMed, EMBASE and the Cochrane Library databases. The search was restricted to articles in English.

Study selection: the review included randomised controlled trials (RCTs) that analysed the impact of VD supplementation during pregnancy on the risk of respiratory tract infection and/or wheezing in the offspring. It also included observational studies on the association between serum levels of 25-hydroxyvitamin D during pregnancy or at birth and respiratory tract infection and/or wheezing in the offspring.

Data extraction: two authors reviewed the selected articles. The quality of the studies was assessed by means of the Cochrane Collaboration Risk of Bias Tool in case of RCTs, and the Effective Public Health Practice Projects Quality Assessment Tool in case of observational studies. The authors performed a meta-analysis of the RCTs that provided data on the effects of VD supplementation during pregnancy on offspring wheezing up to age 5 years. The protocol was registered on PROSPERO.

Results: of the 55 eligible articles, four RCTs were selected, one of which showed a significant reduction in the incidence of respiratory tract infections (16%) and medical visits

(1.5 visits) with high daily doses of vitamin D (2000 IU) during pregnancy and supplementation with 800 IU/day in infants until age 6 months. The meta-analysis of the other three RCTs showed a decreased risk of wheezing when mothers received vitamin D supplementation during pregnancy (relative risk [RR], 0.81; 95% confidence interval [95 CI], 0.68 to 0.97; *P* = .025). The observational studies were heterogeneous and generally showed an inverse association between levels of 25-hydroxyvitamin D in pregnant women or umbilical cord blood and the presence of wheezing and/or respiratory disease in the offspring.

Conclusion: supplementation with high-dose vitamin D during pregnancy is associated with a small decrease in the risk of wheezing of the offspring in the first years of life.

Conflicts of interest: the authors disclosed no conflicts of interest.

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COMMENTARY

Justification: there is an extensive and growing body of scientific literature on the potential role of VD in immune regulation, and an association between VD levels and the risk of infectious disease has been described. A systematic review has shown that VD supplementation decreases the risk of respiratory tract infections both in children and adults, although the most efficacious and safe dosing regimen has yet to be established, and the size of the expected effect remains unclear.[1] There is also evidence that maternal VD levels can influence the levels in newborns. One meta-analysis reported that children of mothers with low VD levels are at greater risk of eczema, but not of wheezing or asthma.[2] Thus, it does seem appropriate to assess whether maternal VD supplementation can be beneficial to the child.

Scientific rigour or validity: the review had clearly defined objectives as to the population of interest, the intervention-exposure and the outcome measure. The search had limitations, since it excluded articles in languages other than English and did not explore clinical trial registers or assess for potential publication bias. The inclusion of observational studies allowed the evaluation of the consistency of the results, although the meta-analysis only included data from experimental studies. The authors assessed the quality of the studies; the only RCT with a risk of bias was not included in the meta-analysis because it did not contribute data on wheezing. Although the review did not find statistical heterogeneity, the pooled RCTs used variable supplementation regimens (from 800 to 4000 IU, starting at 10, 24 or 27 weeks' gestation) and had slightly different outcome measures (at least one episode, recurrent episodes, or persistent wheezing). We need to take into account that none of the pooled RCTs found statistically significant differences.

Clinical relevance: vitamin D supplementation during pregnancy is associated with a 19% reduction in the risk of wheezing in the offspring during early childhood; this estimate is not very precise (RR, 0.81; 95 CI, 0.68 to 0.97). Approximately 20 pregnant women would need to be treated with high-dose VD to prevent one case of wheezing or persistent wheezing (estimated based on the absolute risk reduction for RCTs, which ranged between 4% and 6%).* The efficacy of this intervention seems clinically relevant, although its efficiency and especially its safety need to be evaluated, as it requires daily supplementation at high doses for several months.

Applicability to clinical practice: the applicability of these results to our clinical practice is conditioned by several factors: 1) none of the RCTs analysed was able to prove the efficacy of the intervention; 2) the estimate of the effect size was not precise; 3) there is no clear evidence on which is the safest and most appropriate VD regimen, and 4) differences in nutrition and sunlight exposure between different populations may affect the response to supplementation. Therefore, until further research confirms its efficacy and safety, we cannot recommend high-dose vitamin D supplementation in pregnancy except in women with a clear VD deficiency.

Conflicts of interest: the authors of the commentary have no conflicts of interest to declare.

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* Data calculated by the reviewers using the original data.