

A DIFFERENT VIEW

More data are needed about vitamin D supplements in pregnancy and infancy including any impact on allergies

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1 | INTRODUCTION

The rising prevalence in allergies over the last few decades appears to be a global epidemic. Although we still lack a concise, robust model to adequately interpret this phenomenon, the available evidence points to the role of an increasingly urban and westernised lifestyle. This includes vitamin D deficiency, which is due to staying indoors most of the time without adequate exposure to sunlight and has been identified as one of the contributing risk factors in rising allergy rates. Indeed, a growing body of evidence has suggested that vitamin D deficiency is implicated in the pathogenesis of allergic disorders, although its role is not clear and is open to debate. Vitamin D prophylaxis has already produced excellent results in other areas, for example in reducing the prevalence of rickets.

Accumulating epidemiological evidence has suggested that a lack of vitamin D is a real global problem and knowledge has been emerging on the pleiotropic effects of vitamin D, which is when one gene influences two or more seemingly unrelated phenotypic traits.

In 1991, the European Union issued Commission Directive 91/321/EEC, which recommended that all baby food should be supplemented with vitamin D. Furthermore, many scientific bodies and research groups currently recommend that both pregnant mothers and infants receive vitamin D supplements. Part of the reasoning behind this is based on the results of a number of studies, mainly observational research, that indicate that a lack of maternal and neonatal

vitamin D poses a risk for the development of allergic disorders, such as asthma and atopic dermatitis.

1.1 | Randomised controlled trials on vitamin D supplements

However, it should be noted that, despite the abundance of literature on vitamin D, there have only been a few randomised controlled trials (RCT) that have addressed the issue of vitamin D deficiency in prenatal or early life and its association with the development of allergies. A post hoc analysis of an RCT that examined the vitamin D dose needed to achieve normal levels during infancy showed that supplements during pregnancy and infancy reduced the proportion of children sensitised to house dust mites at 18 months of age.¹ Two larger RCT failed to show a significant reduction of recurrent wheeze and asthma in early childhood following prenatal vitamin D supplements.^{2,3} A potential beneficial effect was only shown when the data from both studies were combined and analysed together.⁴ However, the two studies had different designs and the combined analysis had substantial inherent drawbacks, as all meta-analyses do. In addition, a post hoc analysis⁵ of one of the above-mentioned RCTs² suggested that the protective effect of prenatal vitamin D supplements was only evident in mothers with high levels of 25-hydroxyvitamin D (25(OH)D) at trial entry. The debate continues on whether this may represent a true pharmacological action of vitamin D. We have to bear in mind that such an association may be a mere coincidence,

since entry levels of 25(OH)D were not a planned variable of interest in this study.

1.2 | Evidence against vitamin D supplements

A number of birth cohort studies have addressed the issue from a different viewpoint and have reported a higher prevalence of allergic disorders after vitamin D supplements. These have posed questions that deserve answers that are conclusive and based on evidence. The Northern Finland 1966 Birth Cohort Study found that at 31 years of age the prevalence of atopy, allergic rhinitis and asthma was significantly higher in the 6748 subjects who had received vitamin D supplements regularly during the first year of life than in the 900 who had not. The observed associations were attenuated, but remained significant, after the data were adjusted for a wide range of behavioural and social confounders.⁶ A small Swedish cohort study of 123 subjects found a positive relationship between the estimated average daily dietary intake of vitamin D during infancy and atopic dermatitis at the age of six years. The relationship was independent of any family history of atopic illness.⁷ A UK study found that when the mothers consumed high levels of 25(OH)D during pregnancy, this posed a possible risk factor for allergic disease development in their children at nine years of age. In particular, the children born to the 111 mothers whose 25(OH)D levels were >75 nmol/L during pregnancy were more likely to develop atopic eczema at nine months and asthma at nine years of age than the 111 children born to mothers whose 25(OH)D levels were below 30 nmol/L.⁸ A study of 378 mother-child pairs showed that maternal and cord blood 25(OH)D levels were positively associated with the development of food allergies and sensitisation against food allergens during the first two years of life.⁹ In addition, there was a negative correlation between the cord blood 25(OH)D levels and the number of regulatory T cells, which implied that vitamin D repressed immune tolerance. This latter finding provides a pathophysiological insight that supports the aforementioned studies and was also demonstrated in an earlier birth cohort study with 568 subjects.¹⁰

2 | CONCLUSION

Our current level of knowledge about the effects of vitamin D supplements on allergic disorders is limited. This makes it difficult to explain why both insufficient levels of vitamin D and vitamin D supplements have both been linked to allergic disorders. Maybe, both effects are compatible and the answer lies with the epigenetic modulation of genes in pregnancy and early infancy, where both low and high levels of vitamin D could lead to similar results in a U-shaped association with allergy risk. These vague conclusions mean that vitamin D supplements should probably only be offered to pregnant women who have a deficiency, rather than

as a matter of course to all mothers to be. However, this tactic would not be realistic for young infants, because this would require repeated blood sampling to adjust their level of vitamin D supplements, which would not be desirable or practical. The only safe conclusion that can be drawn about vitamin D supplements in pregnancy and infancy is that we need more data to reach more robust conclusions.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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