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Vitamin D

Vitamin D in pregnancy: an old problem still to be solved?

A F Williams

Perspective on the paper by Dijkstra *et al* (***see page 750***)

In this issue Dijkstra *et al* describe the high incidence of hypovitaminosis D (serum 25-hydroxyvitamin D <25 nmol/l) amongst infants born in Rotterdam, the Netherlands (latitude 52°N). Babies born to veiled or dark-skinned mothers were significantly more likely than those of white mothers to have a low 25-hydroxyvitamin D (25OHD) concentration in umbilical cord blood. Similarly, a recent study of pregnant women in the Hague found that 56–66% of women of Moroccan and Turkish descent had 25OHD levels <25 nmol/l, compared with 8% of women of Western origin.[1] Given that mainland United Kingdom lies at a latitude of 50°–58°N and the populations of its large cities show similar ethnic and cultural diversity, these findings are very relevant to Britain. Indeed amongst Cardiff women from ethnic minority groups attending their first antenatal appointment, half showed a serum 25OHD concentration <20 nmol/l.[2] Those of Indian or African origin were most likely to be affected, especially women who had arrived in the UK within the last 3 years. Interestingly these problems are not confined to northerly latitudes but occur in sunnier climes as well.[3]

We have known for over 30 years that hypovitaminosis D is common amongst pregnant women in ethnic minority groups, particularly those of Asian origin.[4] Intervention studies, including a randomised placebo-controlled trial (amongst women of south Asian origin living in South London) showed that infants of vitamin D supplemented mothers were less likely to be small for gestational age, less likely to develop neonatal hypocalcaemia, and had better tooth enamel mineralisation.[5 6] Recent epidemiological data have added another perspective to maternal vitamin D status in pregnancy and challenge the widely held assumption that suboptimal vitamin D status in pregnancy is a problem confined to at risk ethnic groups. Amongst white women living in Southampton (at one of the most southerly latitudes of the United Kingdom) maternal 25OHD concentrations in the third trimester of pregnancy correlated significantly with the child's whole body and lumbar spine bone mineral content at the age of 9. Eighteen per cent of these mothers showed a 25OHD concentration <28 nmol/l at parturition. Although no national data exist for pregnant women, the low status of UK women of childbearing age is borne out by the National Diet and Nutrition Survey of British adults: 28% of women aged 19–24 and 13% of those aged 25–34 had plasma 25OHD concentrations <25 nmol/l. These findings suggest that infants who present clinically with vitamin D deficiency, either in the neonatal period or later with clinical rickets, represent only a small proportion of those with suboptimal vitamin D status.

How can the risk of vitamin D deficiency in pregnancy, and by implication in infancy, be reduced? In 1991 the Committee on Medical Aspects of Food and Nutrition Policy (COMA) set a reference nutrient intake (RNI) of 10 µg/day (400 IU/day) vitamin D for women who are pregnant or breast feeding.[7] This amount was chosen as sufficient to maintain plasma 25OHD >20 nmol/l during the winter months in Scotland and was endorsed by COMA as recently as 1998.[8] Whilst sunlight exposure is generally of greater importance than diet in the maintenance of vitamin D status, there is no ambient ultraviolet light of the appropriate wavelength at UK latitudes during the winter months. For this reason maintenance of adequate vitamin D status in pregnancy is best achieved through dietary means. However, the average dietary vitamin D intake of young women in the UK approximates 3 µg/day and fewer than 1% consume more than the 10 µg RNI.[9] Achieving the RNI therefore necessitates supplementation. The advice applies to all women and not merely those in ethnic minority groups, yet very few women take a vitamin D supplement during pregnancy and an individual woman's risk of deficiency in pregnancy seems rarely to be assessed.

Unfortunately there have been many barriers to policy implementation. These

include a lack of public and professional awareness, limited availability of suitable supplements which omit retinol (vitamin A) and inconsistency in guidance. In 2003 NICE concluded that "vitamin D supplementation should not be offered routinely to all pregnant women".[10] This view clearly conflicts with the COMA opinions cited above and was based on a meta-analysis of two randomised trials, one of which was conducted in the UK and showed important effects.[5] The Department of Health later stressed the continued importance of offering vitamin D supplements to pregnant women, particularly those in vulnerable groups.[11]

Some time ago a public education campaign conducted amongst at risk groups in Glasgow demonstrated effectiveness in terns of both increased uptake of supplements and a reduction in rickets,[12] but a recurring and commonly cited concern has been the lack of a suitable low cost and palatable preparation. Fortunately this has recently been rectified in the process of reforming the welfare food scheme as *Healthy Start*. A single tablet providing vitamin D (10 µg) with folic acid (400 µg) and vitamin C is now available free to pregnant or breastfeeding mothers who are eligible for *Healthy Start* benefits, and can be prescribed at low cost for those who are not.

The issue of hypovitaminosis D in pregnancy must also recognise current uncertainty about the meaning of "normal" in the context of vitamin D status. Population reference ranges are influenced by a number of biological and lifestyle influences, most importantly sunlight exposure. However, in the twenty first century "sun shy" culture of industrialised nations[13] they may not be indicative of optimal health. Indeed 25-OHD concentrations encountered in people liberally exposed to sunlight (such as lifeguards) exceed by 5–10-fold the lower limit of "normal" (25 nmol/l) cited above.[13] Several authorities in the United States now argue that maintenance of a 25OHD concentration above 75–80 nmol/l is associated with improved health, citing the associated reduction in parathyroid hormone concentration and increased calcium absorption and bone mineral density.[13 14] Interestingly, the achievement of such plasma levels through high dose supplementation (50 µg, 2000 IU vitamin D per day) in breastfeeding mothers also increases both antirachitic activity in breast milk and plasma 25OHD concentration in their infants.[15 16] The National Diet and Nutrition Survey of British adults suggests that if such a threshold were applied to UK population data, some 80–90% would be considered at risk of deficiency.[17] This is potentially therefore a population health issue of considerable importance and its significance and implications require careful thought.[18] Currently the 25-OHD concentration of <25 nmol/l cited by Dijkstra *et al* as a threshold of deficiency risk remains widely adopted but may prove conservative to say the least.

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Vitamin K deficiency

Vitamin K deficiency bleeding: the readiness is all

Paul Clarke, Martin J Shearer

Perspective on the papers by Busfield *et al* and McNinch *et al* (***see pages 954 and 959***)

Over 10 years ago, William Hathaway described the 50-year chequered history of the association between a neonatal bleeding disorder and vitamin K deficiency and its prevention as a splendid example of the cyclical nature of discovery–rediscovery in medical science.[1] The lessons that should have been learnt from the extensive body of early work were reiterated in a recent lively review in this journal.[2] In the UK these forgotten lessons first resurfaced in a 1983 *Lancet* article entitled "Haemorrhagic disease of the newborn returns".[3] Of course this rare deficiency syndrome, now more accurately termed vitamin K deficiency bleeding (VKDB), had never gone away but had merely been rediscovered at a time of a progressive trend towards exclusive breast feeding. The latter had long since been established as an important risk factor for neonatal hypoprothrombinaemia.[4]