Executive summary

The effectiveness and cost-effectiveness of interventions to promote an optimal intake of Vitamin D to improve the nutrition of preconceptional, pregnant and post-partum women and children, in low income households.

This review was carried out in April 2006 – July 2006 by the National Collaborating Centre for Women's and Children's Health

Background

Vitamin D is essential in the maintenance of skeletal growth and bone health. Dietary sources are few and synthesis of vitamin D is dependent on skin exposure to sunlight. The Department of Health recommends that an adequate vitamin D status should be achieved from exposure of the skin to summer sunlight, although this needs to be balanced against increasing the risk of skin cancer. Despite current advice from COMA that vitamin D supplements should be taken by all pregnant and breast-feeding women and their children, up to the age of five, uptake of vitamin D supplementation is low and vitamin D deficiency has re-emerged in recent years as a public health concern, affecting both Asian and Caucasian women in pregnancy, and their children.

The National Diet & Nutrition Survey reported that about 28% of the UK female population aged 19 to 24 years had low serum vitamin D levels (below 25 nmol/l) indicative of vitamin D deficiency. Infants, toddlers and adolescents in 'at risk' ethnic minorities (Asian, African Caribbean and Middle Eastern) are particularly likely to be vitamin D-deficient or to have rickets. In this group, vitamin D deficiency is estimated to occur in around 50% of pregnant women and their neonates, 40% of toddlers, 45% of schoolchildren and over 70% of adolescents. Factors which contribute to this vulnerability include: skin pigmentation, cultural and religious practices such as extensive body covering, exposure to sunlight, spending a limited time outdoors and a vegetarian diet. A 2002 survey of paediatricians in the West Midlands reported an incidence of rickets of 38, 95 and 0.4 per 100,000 per annum in Asian, black and white children aged 0-5 years respectively. Exclusively breastfed infants of mothers who are vitamin D deficient are more likely to be deficient than formula-fed infants because all formula feeds in the UK are vitamin D fortified.

Research questions

The research questions for this review were as follows:

- What public health interventions are effective in promoting an optimal dietary Vitamin D intake (i.e. which meets the intake recommended by COMA) in the following? :

    - women planning a pregnancy
    - pregnant women
    - post-partum women (up to one year following birth) with consideration given to future pregnancies
    - infants and young children from birth and up to five years, both breastfed (fully or partially) and formula fed
    - vulnerable groups, with particular emphasis on lower socio-economic groups, including young teenage mothers, refugees and asylum seekers, black and minority ethnic groups with emphasis on their cultural and religious practices

- What interventions are effective in promoting advice and/or increased uptake of vitamin D supplementation in these population groups? What are the barriers to uptake?

- What practices other than supplementation affect vitamin D status in at risk groups and how can they be modified?

Interventions to promote an optimal dietary vitamin D intake included:

- Vitamin D supplementation
- dietary advice/counselling/education on vitamin D
- intervention to deliver the above dietary advice/counselling/education about vitamin D to mothers, and others, with responsibility for feeding infants and young children in a range of childcare settings
- intervention to improve nutritional knowledge of vitamin D among parents and practitioners
- intervention to improve access of families with infants to food sources rich in vitamin D pre-cursors
- intervention to improve compliance with nutritional advice
- any interventions or practices other than supplementation which may affect vitamin D status in at-risk groups, for example
    - peer support
    - psychosocial interventions such as self-assertiveness skills to improve healthy eating
    - approach which aims to balance the need for safe exposure to sunlight against the risk of skin cancer
    - media campaign

Corroborative evidence related to the process and the context of the interventions, such as the components: development, content, structure, setting, mode of delivery, acceptability, characteristics of the intervener and recipient, and any unintended harmful effects of the intervention were considered.

The review included all public health type interventions that can be delivered by practitioners at the primary care level and in the broader community. In addition, some of the interventions may be carried out by mothers, fathers and carers of infants and young children.

Methods

A systematic review was conducted. Medline, Embase, Cinahl, CCTR, CDSR, DARE and AMED bibliographic databases were searched from 1966 to 2006, using a sensitive strategy that combined relevant terms relating to preconceptional, pregnant and post-partum women, and children with appropriate vitamin D terms. The search was not limited by study type; but was restricted to studies in developed countries and in the English language only. Reference lists of identified articles were also checked.

One reviewer screened titles and abstracts according to inclusion criteria, reviewed retrieved papers, extracted data and appraised quality of eligible studies. Any discrepancies were resolved by discussion with another independent reviewer. Data were entered into evidence tables using the NCC-WCH Access database. Summary statistics and descriptive summaries of the outcomes were presented for individual studies when appropriate.

Results

The search strategy found 4691 potential eligible reports (4647 from electronic searches and 44 from bibliographic search of reference lists of included studies), of which 207 papers were retrieved for further examination. After full text review, 22 papers reporting on 17 studies, conducted between 1976 and 2004, met the inclusion criteria and were included in this review.

Effectiveness of stand alone vitamin D supplementation

Four UK studies conducted between 1976 and 2002 (Brooke et al. 1980 & 1981; Cockburn et al. 1980; Datta et al. 2002) were identified which assessed the effectiveness of stand alone vitamin D supplementation in the prevention of vitamin D deficiency. Furthermore, three RCTs were conducted in Europe (Mallet et al. 1986; Delvin et al. 1986; Ala-Houhala, 1985) and three RCTs in the USA (Greer & Marshall, 1989; Greer et al. 1981 & 1982; Hollis & Wagner, 2004).

All studies showed that antenatal vitamin D supplementation is effective in improving the vitamin D status of Asian and Caucasian women at delivery. Maternal serum 25 OHD concentrations (25 hydroxy vitamin D) were consistently higher in women supplemented with vitamin D during pregnancy compared to those with no supplementation. No adverse effects were reported with vitamin D supplementation to mothers or infants in the two RCTs conducted in the UK.

Evidence statement 1

Evidence from ten studies (eight 1+RCTs and two 2+ studies) show that antenatal vitamin D supplementation is effective in improving the vitamin D status of Asian and Caucasian women.

Infants of mothers who received an antenatal vitamin D supplement achieved a higher body weight during the first year after birth than infants of mothers who received no antenatal vitamin D supplement (Brooke et al. 1980 & 1981). Two UK RCTs by Brooke et al. 1980; 1981 found that at three months the weighted mean difference (WMD) was 0.25; 95% CI 0.05 to 0.45), six months (WMD 0.47; 95% CI

0.25 to 0.69), nine months (WMD 0.25; 95% CI 0.04 to 0.46) and at 12 months (WMD 0.41; 95% CI 0.18 to 0.64), resulting in a significant incremental increase in weight over the 12 months (6.39 ± 0.78 vs. 5.92 ± 0.92; WMD 0.47, 95% CI 0.16 to 0.78).

Evidence statement 2

Evidence from two RCTs indicates that infants of mothers who received an antenatal vitamin D supplement achieved a higher body weight during the first year after birth than infants of mothers who received no antenatal vitamin D supplement.

A non-RCT (2+) study (Cockburn et al. 1980) conducted in the UK found that formula-fed infants had significantly higher 25 OHD concentrations ($p<0.01$) than breast-fed infants, supplemented or un-supplemented at day six. Furthermore, a 1+ RCT undertaken in France (Delvin et al. 1986), reported higher serum 25 OHD levels in breastfeed infants of supplemented mothers compared to breastfeed infants of un-supplemented mothers, at birth and at four days of age. However, a 1+ USA RCT (Greer & Marshall, 1989) reported no significant difference in mean body weight (g) at six months between supplemented (400 IU/day [10 ug/day]), un-supplemented breastfed and formula fed infants (7570 ± 858 – supplemented breastfed vs. 7752 ± 1182 - un-supplemented breastfed vs. 7633 ± 1002 – formula fed infants).

Evidence statement 3

A 2+ study found that breast-fed infants of supplemented (400 IU/day [10 ug/day]) and non-supplemented mothers had lower serum 25 hydroxy vitamin D concentrations than formula-fed infants six days after delivery.

Evidence statement 4

There is 1+ evidence to suggest that supplemented breastfed infants (1000 IU/day [25 ug/day] during the 1st trimester) achieved a higher serum 25 hydroxy vitamin D levels than un-supplemented breastfed infants, at birth and at four days of age.

Evidence statement 5

Evidence from a 1+ study indicates that the weights of supplemented (400 IU/day [10 ug/day]), un-supplemented breast-fed infants and formula-fed infants did not differ at six months.

Evidence from two RCTs (Greer et al. 1981 & 1982; Greer & Marshall, 1989) indicates that the effect of vitamin D supplements on infant bone mineral content is uncertain. A study by Greer et al. (1981 & 1982) found that Vitamin D supplemented breast-fed infants (400 IU/day [10 ug/day]) had a higher bone mineral content than un-supplemented infants at 12 weeks and 6 months but not at six weeks. However in contrast to these findings, a later RCT by Greer & Marshall (1989) found that un-supplemented breastfed infants were found to have a measured bone mineral content significantly higher than supplemented breastfed infants (101 ± 17.9 vs. 89.5 ± 12.5, $p<0.05$) at six months. This is despite the supplemented breastfed infants having a higher serum 25 OHD concentration.

Evidence statement 6

Evidence from two 1+ RCTs indicates that the effect of vitamin D supplements on infant bone mineral content is uncertain. The results from two studies were found to be conflicting.

Effectiveness of interventions to promote optimal dietary intake of vitamin D

The literature search (1990 to 2006) did not identify any studies, which evaluated the effectiveness of interventions to promote optimal dietary intake of vitamin D, or any published intervention programmes which aimed to promote optimal uptake of vitamin D, in the UK or other developed countries.

Expanding the search back to 1966, four intervention programmes (Box, 1983; Dunnigan et al. 1981 & 1985; Henderson. 1989; Save the Children Fund. 1983) were identified, carried out in the UK between 1979 and 1989. The quality of reporting in these studies was found to be generally poor with insufficient details provided. The target populations in these studies included Asians of all ages (adults 19-70 years and children 0-18 years).

A five month health education campaign (2-) by community health professionals to prevent vitamin D deficiency in Glasgow, by Asian link workers to Asian women aged 19-60 years, which provided vitamin D supplements at cost price did not increase their serum 25 OHD concentrations one to two years after the campaign. The uptake of vitamin D supplements fell when home visits stopped and the sale of vitamin D fell two to three years after the campaign. The number of patients discharged from hospital with rickets and osteomalacia was reduced (Henderson, 1989).

A health education campaign (2-) to prevent vitamin D deficiency by community health professionals to Asians in Glasgow provided free vitamin D supplements on demand for children aged 0-18 years. The campaign increased their serum 25 OHD concentrations, reduced the number of discharges from hospital with nutritional rickets and increased the number of vitamin D supplements dispensed two to three years after the campaign (Dunnigan et al. 1981 & 1985).

A 2- health education campaign by a charity organisation and voluntary Asian groups (with UK government support) was identified which aimed to prevent vitamin D in twenty five area Health Authorities (Save the Children Fund, 1983). The campaign improved knowledge scores about vitamin D deficiency and importance of vitamin D supplements, one year after the campaign. No other outcomes were assessed.

A 1- quasi RCT (Box, 1983) which provided dietary advice by a health visitor at an antenatal clinic had a very small effect in improving vitamin D dietary intakes and no effect on serum 25 OHD levels in Asian pregnant women at 4 months.

Reporting of the process-related corroborative evidence of the health education interventions was poor with little details on the infrastructure, approaches, strategy and delivery mechanism of the interventions.

Evidence statement 7

There is 1- and 2- evidence to suggest that health education programmes on the prevention of vitamin D deficiency had the potential to improve the knowledge base about vitamin D, increase the uptake of vitamin D supplements and reduce the number of hospital admissions with rickets and osteomalacia.

The review did not identify any intervention studies, which aimed to improve the vitamin D status of women specifically at the pre-conceptional period, nor in women and children in low income households. nor any intervention studies which assessed the effect of sunlight exposure on the vitamin D status of women.

Furthermore, no studies of good quality were found which addressed the following:

- intervention to improve access of families with infants to food sources rich in vitamin D pre-cursors
- intervention to improve compliance with nutritional advice
- any interventions or practices other than supplementation which may affect vitamin D status in at-risk groups, for example
    - peer support
    - psychosocial interventions such as self-assertiveness skills to improve healthy eating
    - approaches which aimed to balance the need for safe exposure to sunlight against the risk of skin cancer
- Corroborative evidence related to the process and the context of the interventions, such as the components: development, content, structure, setting, mode of delivery, acceptability, characteristics of the intervener and recipient, and any unintended harmful effects

Conclusions

There are important limitations in the evidence reviewed in its paucity, currency and quality. There is a dearth of up-to-date robust evidence to answer the research questions. Interpretation of available evidence and direct application of findings to the current susceptible target populations should therefore be considered with caution. Variations in regional latitudes, sunlight exposure, ethnicity, culture, dietary and dress habits, language barriers, access to health care, food fortification policy and adherence to the public health advice on sun protection are likely to influence outcomes and compound the problem of vitamin D deficiency.

Health education programmes, which showed an increase in knowledge about rickets and uptake of supplements, may not be sufficient grounds on which to base health policy. The interventions should demonstrate an improvement in health. Campaigns based on health education or the provision of vitamin D supplements need to be compared with doing nothing at all, as spontaneous recovery has been reported to occur in vitamin D deficient Asian children over the summer months. It has been suggested that the differences in vitamin D status among white and non-white individuals may be better explained by the amount of sunlight exposure and degree of body coverage than by dietary vitamin D intake. What constitutes an adequate dose of sunlight exposure to satisfy the body's requirement for vitamin D may be difficult to determine for every individual and this question is outside the scope of this review. To strike a balance between the health risks of vitamin D deficiency and skin

cancer, public health advice and recommendations on sun protection may need to be moderated.

The sub clinical nature of vitamin D deficiency may be difficult to detect in asymptomatic individuals, thus delaying diagnosis and treatment. Education and training to improve knowledge of public health professionals about vitamin D deficiency among vulnerable groups are needed.

Future intervention studies should employ a robust research methodology with appropriate evaluation tools to assess the effectiveness of the interventions.

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