Effect of maternal calcium intake during pregnancy on children's blood pressure: a systematic review of the literature

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CRD summary
This review summarised published evidence on the association between maternal dietary calcium intake during pregnancy and blood-pressure in the offspring. The authors concluded that there is evidence to support such an association, but more research is needed to confirm it. Despite the potential for bias in the review methods, these cautious conclusions appear reasonably reliable on the basis of the presented evidence.

Authors' objectives
To summarise the evidence on the association between maternal dietary calcium intake during pregnancy and blood-pressure (BP) in the offspring.

Searching
MEDLINE, EMBASE and the Cochrane Library (Issue 4, 2005) were searched from 1966 to December 2005; the search terms were reported. The reference lists of retrieved studies and reviews were examined for further relevant papers.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and observational studies were eligible for inclusion in the review. Ecological studies and studies with historical controls were excluded.

Specific interventions included in the review
Studies evaluating maternal dietary calcium intake during pregnancy via food or supplementation were eligible for inclusion in the review. Where reported, approximately 2 g/day calcium was administered in the form of calcium carbonate.

Participants included in the review
Studies evaluating outcomes in the offspring of mothers whose calcium intake was assessed during pregnancy were eligible for inclusion in the review. The age of offspring at follow-up ranged from birth to 9 years.

Outcomes assessed in the review
Studies measuring the systolic and diastolic BP in the offspring or the incidence of hypertension were eligible for inclusion in the review.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality
The validity of RCTs was assessed according to the method described in the Cochrane Handbook for Systematic Reviews of Interventions; observational studies were assessed according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the extraction. Data were extracted on crude and adjusted (including list of variants adjusted for) effect sizes, with corresponding confidence intervals (CIs) and p-values. Calcium intake was also extracted and converted to the amount of elemental calcium in milligrams. Standard errors were calculated for correlation coefficients using the Fisher r-to-z transformation. Correlation coefficients were converted to standardised mean differences (SMDs) and multiplied by BP
standard deviation to estimate the size of the effect.

**Methods of synthesis**

How were the studies combined?
Individual SMDs were combined using meta-analysis, supplemented with a narrative summary. A funnel plot was constructed to assess publication bias.

How were differences between studies investigated?
Heterogeneity between the study results was assessed using the chi-squared and I-squared statistics, the results of which were used to stratify by age.

**Results of the review**

Five studies (n=7,225) were included in the review: 2 RCTs (n=5,783) and 3 observational studies (n=1,442).

The small number of included studies meant that the funnel plot was not informative, so publication bias could not be excluded. Loss to follow-up was considerable in 4 of the 5 included studies.

There was greater heterogeneity among studies conducted in children under 12 months of age (I-squared 53%) than those conducted in older children (I-squared <10%). Studies were therefore stratified by age, with only studies in children aged over 12 months (4 studies: 2 RCTs, 2 observational studies) being statistically pooled. These gave a pooled estimate of a -1.92 mmHg reduction (95% CI: -3.14, -0.71) in offspring systolic BP associated with calcium intake.

Three heterogeneous studies (1 RCT, 2 observational studies) in children aged less than 12 months all showed generally favourable effects on offspring systolic BP, though only two of these effects (both from observational studies) were statistically significant.

**Authors’ conclusions**

There is published evidence to support an association between calcium intake during pregnancy and the offspring’s BP. However, more research is needed to confirm these findings.

**CRD commentary**

This review was based on a well-defined question that was supported by appropriate inclusion criteria. Attempts were made to identify relevant publications by searching major electronic sources and checking reference lists, though no attempt was made to identify unpublished literature and it is not clear whether the search was restricted by language of publication. Some relevant studies may therefore have been missed, potentially introducing publication bias. It is also unclear whether the authors took any steps to minimise the potential for reviewer error and bias in the selection of the primary studies and extraction of data. The validity of the included studies was assessed according to established standards, and relevant details of these studies were presented in the review. It should be noted that, though apparently statistically homogeneous, studies included in the meta-analysis varied in terms of their populations (e.g. age of children) and study designs. However, the authors’ conclusions provide a reasonably accurate summary of the retrieved evidence and the additional research required to supplement this evidence.

**Implications of the review for practice and research**

Practice: The authors did not state any implications for practice.

Research: The authors stated that further evidence is needed from the long-term follow-up of large well-conducted RCTs of calcium supplementation during pregnancy. They added that more studies in populations with calcium deficiencies and assessing the effects on cardiovascular risk factors other than BP are needed.

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