Meta-analysis: Calcium supplementation reduces blood pressure and preeclampsia during pregnancy


Objective
To evaluate the effect of calcium supplementation during pregnancy on blood pressure (BP), preeclampsia, and adverse outcomes.

Data sources
Studies were identified by searching the MEDLINE and EMBASE databases using the keywords calcium and hypertension or blood pressure; a Cochrane Collaboration search strategy, developed to enhance retrieval when conducting systematic reviews, was also used. Further searching was done using MEDLINE and EMBASE (1966 to May 1994) with key and text words identified from retrieved citations. Authors of eligible studies were contacted to help identify unpublished trials.

Study selection
Studies were selected if they included pregnant women who were randomised to receive or not receive calcium supplementation and if their BP was measured. Studies were excluded if they had < 2 weeks of intervention or if data from the same patients were included in previous reports.

Data extraction
Extracted data included number of patients, calcium formulation, weeks of gestation, treatment duration, mean change in BP, and incidence of preeclampsia. Reviewers worked independently in pairs while extracting data and assessed the validity of each study according to 6 quality criteria.

Main results
14 trials involving 2459 women met the selection criteria. The pooled analysis of all studies showed a reduction in systolic BP of -5.40 mm Hg (95% CI -7.81 to -3.00 mm Hg, P < 0.001) and in diastolic BP of -3.44 mm Hg (CI -5.20 to -1.68, P < 0.001). In the pooled analysis, strong evidence of heterogeneity existed for both systolic and diastolic BP. For systolic BP, nulliparous status was associated with a treatment effect. For diastolic BP, nulliparous status, multiparous status, and methodologic quality of the study were associated with a treatment effect. Based on the results of 8 studies, the odds ratio (OR) for hypertension in women with calcium supplementation was 0.30 (CI 0.17 to 0.54). The OR for preeclampsia in women with calcium supplementation compared with placebo was 0.38 (CI 0.22 to 0.65). Based on the results of 9 randomised controlled trials included in this systematic review, the lowest control event rate for preeclampsia is 4%. Assuming a patient's expected event rate of 4%, 41 women (CI 32 to 73) would have to be treated to prevent 1 additional episode of preeclampsia. No statistically significant differences existed between the 2 treatment groups for preterm delivery, intrauterine growth retardation, cesarean section, and perinatal deaths.

Conclusion
Calcium supplementation during pregnancy reduces systolic and diastolic blood pressure and the incidence of preeclampsia and of hypertension.


For article reprints: Dr. G.H. Guyatt, Department of Clinical Epidemiology and Biostatistics, Room 2C10, McMaster University, 1200 Main Street West, Hamilton, Ontario L8N 3Z5, Canada. Ph. 905-577-0017.

Commentary
Preeclampsia and pregnancy-induced hypertension are major causes of maternal morbidity and mortality. Large trials have diminished the initial enthusiasm for using low-dose aspirin in the prevention of these two conditions (1). Calcium is now the new hope.

The excellent systematic review by Bucher and colleagues evaluated the effect of calcium supplementation on the incidence of preeclampsia and hypertension. The study provides the best evidence on this subject to date, and the results support the use of calcium supplementation in pregnant women.

The authors took into account heterogeneity, thus ruling out this source of bias. Also, it is of interest that the treatment effect on mean arterial BP was stronger in the studies in which the outcome assessment was blinded. Of even more importance is that the incidence of hypertension (analysed as a binary outcome) was reduced by calcium supplementation.

Despite the treatment effects on BP, the possibility that calcium supplementation only treated, rather than prevented, hypertension was not ruled out. Also, no conclusive data suggest that fetal morbidity or mortality can be modified. Further, we do have some concern because only 2 trials with > 200 pregnant women were included in this meta-analysis; most were smaller trials.

The results of a meta-analysis (based on small trials) that evaluated the effects of low-dose aspirin on preeclampsia showed an 82% reduction in the incidence of preeclampsia (1). This figure was not confirmed by large trials nor by a second meta-analysis based on large trials (1). Thus, the results of the Calcium for Preeclampsia Prevention Study (2), which are expected within the next few months, are anxiously awaited.

In the meantime, because calcium supplementation is inexpensive and seems to have benefit, it may be a convenient method of preventing preeclampsia and the occurrence of hypertension in pregnant women at risk.

Alvaro Atallah, MD, PhD Escola Paulista de Medicina Sao Paulo, Brazil

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