The safety of nitrofurantoin during the first trimester of pregnancy: meta-analysis

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Authors' objectives
To evaluate the safety of nitrofurantoin (NF) ingested during early pregnancy.

Searching
MEDLINE was searched using the following keywords: 'nitrofurantoin', 'fetal abnormality', 'fetal anomaly', 'malformations', 'teratogenicity' and 'pregnancy'. Standard textbooks were checked for any additional references.

Study selection
Study designs of evaluations included in the review
Cohort and case-control studies (with a control group not receiving NF) were included.

Specific interventions included in the review
NF given as an antibiotic treatment during pregnancy.

Participants included in the review
Pregnant women were included.

Outcomes assessed in the review
The rates of major foetal malformations were assessed.

How were decisions on the relevance of primary studies made?
Two independent investigators made decisions based on the following criteria: human studies of maternal NF exposure in first trimester of pregnancy, with outcomes of major or minor foetal malformation published in any language. The studies were assessed without knowing the results.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the Mantel-Haenszel procedure.

How were differences between studies investigated?
The ORs of 3 of the 4 studies were calculated while omitting a different study each time.

Results of the review
Four cohort studies: 3 retrospective and 1 prospective. In one study, data was from the Motherisk database, i.e. women seen in the authors’ clinic during the first trimester, and for whom pregnancy outcome was verified. The number of patients included was not stated.
No significant differences were found between the study and the control groups (pooled OR 1.29, 95% CI: 0.25, 6.57).

**Authors' conclusions**
The results from the individual studies, and the combined results from all studies together, did not show a significant correlation between exposure to NF and foetal malformations. Although the data are not optimal for meta-analysis, the authors thought it important to evaluate the existing data and combine the different studies in the absence of any prospective study. Prospective controlled studies are urgently needed in order to verify the safety of NF.

**CRD commentary**
Since the search is limited to MEDLINE and the search dates are unclear, it is uncertain how many relevant studies may have been missed. No quality assessment of the included studies is presented and the pooling of results from observational studies is questionable.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.