Aspirin for the prevention of preeclampsia in women with abnormal uterine artery Doppler: a meta-analysis

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Authors' objectives
To assess the effect of aspirin in preventing pre-eclampsia in women identified as being at high risk by an abnormal uterine artery Doppler examination in the second trimester.

Searching
MEDLINE, EMBASE, and the Cochrane Controlled Trials Register were searched for trials published between 1966 and November 2000. A combination of search terms were used to generate two subsets of citations: one including studies of 'aspirin' ('aspirin', 'antiplatelet', 'salicyl', 'acetylsalicyl', and 'platelet aggregation inhibitors') and the other including studies of 'Doppler ultrasonography' ('ultrasonography', 'ultraso*', and 'Doppler'). These subsets were combined using 'and' to generate the final list of citations. The reference lists of known primary studies and review articles were examined, and frequently cited articles were checked in the Science Citation Index for additional relevant papers. Researchers in this field were contacted for further information. No language restrictions were stated.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Comparisons of low-dose aspirin (any definition) with placebo or no drug treatment were eligible for inclusion. The dose of aspirin ranged from 50 to 100 mg/day.

Participants included in the review
Women who had an abnormal uterine artery Doppler assessment in the second trimester were eligible for inclusion. Any definition of abnormality was accepted.

Outcomes assessed in the review
For inclusion, the studies had to assess the proportion of women developing proteinuric hypertension (pre-eclampsia) and the difference in birth weight. The secondary outcomes were non-proteinuric hypertension, small for gestational age (any definition), gestational age at delivery, and foetal or maternal complications.

How were decisions on the relevance of primary studies made?
Two authors independently reviewed the citations for relevance. Those citations deemed definitely or possibly relevant were retrieved in full and two authors then independently assessed the papers for inclusion. Any disagreements were resolved by consensus or by arbitration by a senior reviewer.

Assessment of study quality
The included studies were assessed for methodological quality using guidelines developed by the NHS Centre for Reviews and Dissemination (see Other Publications of Related Interest no.1). Information on the adequacy of randomisation, concealment, control, blinding, intention to treat, and follow-up rates was sought. Two authors independently performed the quality assessment. Agreement between the reviewers was assessed by the percentage agreement and kappa statistic.

Data extraction
Two authors independently extracted the data.
The data were extracted for the following categories: trial identification; setting; gestation at testing; definition of Doppler abnormality; aspirin dose; comparison; and outcomes.

**Methods of synthesis**

How were the studies combined?
The studies were weighted according to the inverse of the variance. Publication bias was assessed using a funnel plot analysis. Pooled odds ratios (ORs), along with 95% confidence intervals (CIs), were calculated for binary data using a fixed-effect model (see Other Publications of Related Interest no.2).

The weighted mean difference (WMD) and the 95% CIs were calculated using a fixed-effect model for continuous variables, using the means and standard deviations from individual studies.

The number-needed-to-treat was also calculated.

How were differences between studies investigated?
Heterogeneity of treatment effects was evaluated using the chi-squared statistic. The tests were designed a priori to explore the causes of heterogeneity using variation in features of the population, intervention, outcome and study quality.

**Results of the review**

Five RCTs with 498 participants (aspirin group = 251; placebo group = 247) were included in the review.

The agreement between the reviewers for decisions on inclusion was 99.7% (kappa = 0.93).

Pooling showed a significant benefit of aspirin therapy in reducing pre-eclampsia (OR ratio 0.55, 95% CI: 0.32, 0.95). The number-needed- to-treat was 16 (baseline risk 16%, 95% CI: 8, 316).

Women on aspirin therapy had babies who were on average 82 g heavier than controls, but this trend did not reach statistical significance (WMD 81.5, 95% CI: -40.27, 203.27). None of the measures for secondary outcomes were statistically significant.

The results were statistically homogeneous.

The funnel plot analysis did not show publication bias.

**Authors' conclusions**

Uterine artery Doppler assessment identifies high-risk women in whom aspirin therapy results in a significant reduction in pre-eclampsia.

**CRD commentary**

The authors stated their research question and the inclusion and exclusion criteria. The literature search was fairly thorough and searched for unpublished data. While language restrictions were not stated, publication bias was assessed and it is unlikely that additional studies were missed. The authors report who, and how many of the authors, performed the selection of studies, quality assessment and data extraction processes.

The statistical pooling used appropriate methods for both binary and continuous data, and heterogeneity was assessed. If heterogeneity had been found, the authors had a priori plans to test for the effects of heterogeneity on the results. The number-needed-to-treat was also presented for the benefit of practitioners.

The authors’ conclusions appear to follow from the results and present a good assessment for the effects of aspirin as a preventative treatment. It should be noted, however, that the conclusions are a little confusing and may be better stated as: 'Uterine artery Doppler assessment identifies women at high-risk for pre-eclampsia. For these women, aspirin
therapy results in a significant reduction in pre-eclampsia.’

Implications of the review for practice and research
Practice: The authors state that, in obstetric units where a routine midtrimester scan for foetal abnormality is already offered, uterine artery Doppler assessment in the second trimester and treatment with aspirin in women who are found to have abnormal Doppler findings, could be added with little additional resource implications.

Research: The authors state that further research is needed to address the possible cost benefits of this approach, and also to examine whether the observed reduction in the incidence of pre-eclampsia translates into improvement in other clinically important outcomes.

Bibliographic details

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Other publications of related interest

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Record Status
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.