Low-dose aspirin: lack of association with an increase in abruptio placentae or perinatal mortality
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Authors' objectives
To determine the association between low-dose aspirin treatment and subsequent abruptio placentae or perinatal mortality.

Searching
MEDLINE was searched from January 1985 to April 1994, using the headings: 'human pregnancy', 'pregnancy-induced hypertension', 'preeclampsia', 'aspirin', 'hypertension', 'clinical trials' and 'abruptio placentae'. Reference lists from all retrieved reports, review articles and chapters from textbooks were examined to locate further trials. Only published, English language literature was considered for inclusion.

Study selection
Study designs of evaluations included in the review
Randomised or double-blind clinical trials were included.

Specific interventions included in the review
Aspirin (less than 200 mg/day), for the prevention of either pre-eclampsia or foetal growth restriction, versus placebo or no treatment.

Participants included in the review
Pregnant women of varying risk status for pre-eclampsia and foetal growth restriction were included.

Outcomes assessed in the review
The incidence of maternal abruptio placentae and perinatal mortality was assessed.

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

Assessment of study quality
The authors do not report a method for assessing validity. However, only randomised or double-blind clinical studies were included in the review. The authors independently evaluated the study methods for each trial.

Data extraction
The authors independently abstracted quantitative outcome data. Authors of the primary studies were contacted for further details if necessary.

Methods of synthesis
How were the studies combined?
For each outcome, the relative risk, risk differences and 95% confidence intervals were calculated.

How were differences between studies investigated?
Chi-squared and Fisher exact tests (two-tailed) were used when appropriate to look at the effects of varying at study entry, and the effects of double-blind versus non-blinded study design.
Results of the review

Eleven randomised controlled trials (RCTs) were included, nine of which were double-blind (n=14,833)

[A: Notice of correction. It has come to our attention that the data in 2 of the 11 references (nos.4 and 12) that met our predetermined meta-analysis criteria may not be valid. We would note that the senior author of these reports did answer our questions, and he provided precise data in written correspondence to us. However, because of this concern, we repeated our meta-analyses without these two publications, and added data from a recent randomised trial in Brazil that also met our criteria. We found results similar to those in our published report. The incidence of abruptio placentae in these 10 trials of low-dose aspirin was 119 out of 7,845 women (1.52%) assigned to aspirin and 102 out of 7,694 women (1.32%) assigned to placebo (x squared, p=0.314 Fischer exact test, two-tailed, p=0.343). Perinatal death occurred in 215 out of 8,038 cases (2.7%) assigned to aspirin and in 212 out of 7,940 cases (2.7%) assigned to placebo (x squared, p=0.0946; Fischer exact test, two-tailed , p=0.961).]

The incidence of abruptio placentae in the 7,493 women randomised to aspirin treatment (1.67%) was similar to that in the 7,430 women randomised to a placebo or no treatment group (1.43%) (p=0.24). Only 2 of the 11 studies reported a statistically significant difference, one showing a reduction in abruptions associated with aspirin and the other an increase with aspirin use.

Review of perinatal mortality in the 11 randomised trials of low-dose aspirin in pregnancy confirmed that the mortality was similar in both groups (p=0.42), with only 1 of the 11 trials reporting a significant benefit in the aspirin group.

Authors’ conclusions

Women assigned to low-dose aspirin during pregnancy have a perinatal mortality similar to those assigned to placebo or no treatment.

CRD commentary

The objective of this review is clearly defined, as are the inclusion criteria. The literature search is well reported but limited in that it only includes English language articles, which may lead to publication bias within the review. The authors give consideration to the appropriateness of pooling data from the included trials due to variations in risk criteria used to qualify for study entry. The authors also comment on the fact that the criteria for the diagnosis of abruptio placentae was not reported in any trial, it was not reported as the primary outcome in any trial, and neither the consistency of the degree of abruption nor a correlation with clinical signs and symptoms or perinatal outcomes could be ascertained from any of the included trials.

Funding

Agency for Health Care Policy and Research, grant number DHHS 282-92-0055.

Bibliographic details


PubMedID

7770254

Indexing Status

Subject indexing assigned by NLM

MeSH

Abruptio Placentae /chemically induced /epidemiology; Aspirin /administration & dosage /adverse effects; Double-Blind Method; Female; Fetal Growth Retardation /prevention & control; Humans; Incidence; Infant, Newborn; Infant, Newborn, Diseases /chemically induced /mortality; Pre-Eclampsia /prevention & control; Pregnancy; Randomized
Controlled Trials as Topic

AccessionNumber
11995001525

Date bibliographic record published
28/02/1999

Date abstract record published
28/02/1999

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.