Systematic review

Updated review identifies no adverse impact on mother or offspring during the perinatal period of aspirin use for prevention of preeclampsia

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Commentary on: Henderson JT, Whitlock EP, O'Connor E, *et al.* Low-dose aspirin for prevention of morbidity and mortality from preeclampsia: a systematic evidence review for the US Preventive Services Task Force. *Ann Intern Med* 2014;160:695–703.

Context

Aspirin is recommended in current international guidelines for women at heightened risk for preeclampsia. Preeclampsia occurs in 2–8% of pregnancies and is a leading cause for both maternal and fetal morbidity and mortality. Effective prevention approaches therefore have the potential for significant health benefits. In 1996 the US Preventive Services Task Force produced a report on the identification, prevention and treatment of preeclampsia, stating:

> There is insufficient evidence to recommend for or against routine aspirin prophylaxis in pregnancy for the prevention of either preeclampsia [...] or intrauterine growth retardation [...]. Clinicians may wish to inform patients at high risk of preeclampsia that aspirin prophylaxis has been shown to decrease this risk, but such patients should also be informed that aspirin has not been proven to improve overall foetal or maternal outcomes, that one large trial raised the possibility of an increased risk of abruptio placentae, and that aspirin can have additional unpleasant and occasionally serious side effects.[1]

To update these recommendations a new systematic review was performed.

Methods

Randomised controlled trials (RCTs) and large observational reports, which studied aspirin use during pregnancy, were identified from publication databases, reference lists and the trials registry clinicaltrials.gov. The review answered three distinct questions: first, is low-dose aspirin effective for reducing adverse maternal and perinatal health outcomes among women at increased preeclampsia risk? Second, does low-dose aspirin prevent preeclampsia in women at increased risk? Third, is there any harm to mother or fetus associated with aspirin use? Heterogeneity and publication bias were assessed. The search strategy, study selection, assessment of study quality, data extraction, interpretation and pooled analysis were consistent with recognised protocols for systematic reviews.

Finding

Twenty-three studies met inclusion criteria; 15 addressed the impact of aspirin on maternal and perinatal health, 13 reported incidence of preeclampsia and 21 assessed the possibility of harm. Aspirin use was associated with a significant reduction in preterm birth (risk ratio (RR)=0.86, 95% CI 0.76 to 0.98) and intrauterine growth restriction (RR=0.80, 95% CI 0.65 to 0.99) with an increase in reported birth weight (130 g, 95% CI 36.22 to 223.33 g). Incidence of preeclampsia was reduced by 24% (RR=0.76, 95% CI 0.62 to 0.95) with no evidence that timing or dosage of aspirin had effects on this outcome. There was no significant evidence of harm, in particular, incidence of placental abruption (RR=1.17, 95% CI 0.93 to 1.48) and postpartum haemorrhage (RR=1.02, 95% CI 0.96 to 1.09) did not differ. Follow-up to 18 months in observational studies did not show evidence of harm to the offspring.

Commentary

The findings are largely consistent with results from a recent Cochrane Collaboration review and the individual patient data analysis performed within the Perinatal Antiplatelet Review of International Studies (PARIS) collaboration.[2 3] All three studies identified a reduction in preterm birth varying from 8% to 14%. However, the 24% reduction in preeclampsia is substantially larger than reported in either the Cochrane study (17%) or the PARIS analysis (10%). The authors suggest this is due to significant small study effects and note more modest findings in the two largest trials, which individually report reductions in RR of 0.88 (95% CI 0.75 to 1.03) and 0.90 (95% CI 0.77 to 1.06). The authors propose a 10% reduction in risk is a more appropriate estimate. Notably these trials, which account for the bulk of reported effect sizes, were performed in the 1990s; therefore, the consistency of recent review findings is entirely expected as all are based on the same available data. Recent trials have tended to involve less than 600 individuals and studied specific refinements of treatment. However, their size means they have little influence on the pooled analysis, and effects related to timing of treatment, dose of aspirin or severity of disease remain difficult to identify.

The change in clinical practice introduced by the trials has meant more information on safety has become available in the past 15 years within both trials and observational studies. From these, the current review has concluded there are no adverse maternal effects and offspring appear to have no change in outcomes up to 18 months of age. This review will generate updated US Preventive Service Task Force recommendations and is reassuring in that the current, more widespread use of aspirin has not led to the identification of any adverse effects during pregnancy or in the immediate postnatal period from aspirin use.

Competing interests None.

Provenance and peer review Commissioned; internally peer reviewed.

References

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3. **Askie LM,** Duley L, Henderson-Smart DJ, *et al.* Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data. *Lancet* 2007;**369**:1791–8.