Review: antiplatelet drugs reduce pre-eclampsia, preterm birth, and stillbirth or neonatal death

Duley L, Henderson-Smart D, Knight M, et al. ***Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review.*** *BMJ 2001 Feb 10;**322**:329–33.*

QUESTION: In pregnant women at risk for pre-eclampsia, how effective are antiplatelet drugs in preventing pre-eclampsia and its complications?

Data sources

Studies were identified by searching the Cochrane Pregnancy and Childbirth Group register of trials, the Cochrane Controlled Trials Register, and EMBASE/Excerpta Medica (1994–9) and by handsearching conference abstracts.

Study selection

Studies were selected if they were randomised controlled trials comparing antiplatelet drugs with placebo or no antiplatelet drug in women at risk for developing pre-eclampsia. Exclusion criteria were having no clinical data available, inadequate randomisation, <80% follow up of patients, or having participants at very low risk for pre-eclampsia.

Data extraction

Data were extracted on study validity (allocation concealment), patient risk for developing pre-eclampsia (high or moderate), length of gestation (< or ≥20 wks), dose of aspirin (≤75 mg or >75 mg), whether the study was placebo controlled, and outcomes (for women: pre-eclampsia, caesarean section, antepartum haemorrhage, serious maternal morbidity, and rare adverse events; for infants: death [stillbirth, neonatal, or infant], preterm birth [<37 wks], small for gestational age, bleeding episodes, and infant development measures).

Main results

39 trials (30 563 women) were included. Most trials (28 802 women) compared aspirin with placebo. Fewer patients receiving antiplatelet drugs had pre-eclampsia than control group patients (table). The relative benefit was not affected by risk status, dose of aspirin, length of gestation at trial entry, or use of a placebo. The groups did not differ for the other maternal outcomes of eclampsia (9 trials), maternal death (2 trials), or caesarean section (17 trials). Fewer preterm births, stillbirths, or neonatal deaths occurred in the antiplatelet drug group (table). The groups did not differ for small for gestational age births (25 trials), intraventricular haemorrhage (8 trials), other neonatal bleeding (6 trials), or infant development (1 trial).

Conclusion

In pregnant women at risk for pre-eclampsia, antiplatelet drugs prevent pre-eclampsia and reduce the risk for preterm birth and stillbirth or neonatal death.

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*Antiplatelet drugs v placebo or no antiplatelet drug for women at risk for pre-eclampsia**

Outcomes at delivery	Number of trials	Weighted event rates		RRR (95% CI)	NNT (CI)
		Antiplatelet	Placebo		
Pre-eclampsia	27	6.8%	7.8%	15% (8 to 22)	100 (59 to 167)
Preterm birth	23	17.2%	18.6%	8% (3 to 12)	72 (44 to 200)
Stillbirth or neonatal death	30	2.5%	2.9%	14% (2 to 25)	250 (125 to >10 000)

*Abbreviations defined in glossary; weighted event rates calculated from data in article.

COMMENTARY

Good biological rationale exists to explain why low doses of antiplatelet drugs should reduce the likelihood of pre-eclampsia, preterm birth, and their perinatal consequences among women at risk for pre-eclampsia. Small, randomised, controlled trials seemed to confirm the hypothesis, but subsequent large trials did not.[1] The discrepancy between the earlier positive results and the later negative ones was attributed to publication bias. In this systematic review and meta-analysis done as part of the work of the Cochrane Collaboration,[2] Duley *et al* have found that antiplatelet drugs confer important and statistically significant benefits on mothers at risk for pre-eclampsia and on their infants, without any identified risks. The review is powerful because it includes studies that are methodologically strong and because the total number of women enrolled is very large (>30 000). The findings of a modest reduction in risk for pre-eclampsia, preterm birth, and death of the fetus or baby with antiplatelet treatment are important. Additional information will come from the pooling of data from the existing trials about the effects of higher doses of aspirin, treatment among higher risk women, and treatment at an earlier point in gestation.

Compelling evidence exists to recommend general and widespread use of low dose aspirin (<75 mg) beginning after 12 weeks of pregnancy for women at risk for pre-eclampsia. The women most likely to benefit are those with a history of pre-eclampsia, chronic hypertension, or such medical problems as diabetes or renal disorders. Women with more moderate risk factors, however, may also benefit (eg, first pregnancy, multiple pregnancy, family history of pre-eclampsia, teenaged mother, abnormal result on uterine artery Doppler scan or rollover test, or mild increase in blood pressure without proteinuria). These women should also be offered this effective treatment.

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1 CLASP 1994 CLASP (collaborative low-dose aspirin study in pregnancy) Collaborative Group. CLASP: a randomised trial of low-dose aspirin for the prevention and treatment of pre-eclampsia among 9364 pregnant women. *Lancet* 1994;**343**:619–29.
2 Knight M, Duley L, Henderson-Smart DJ, *et al.* Antiplatelet agents for preventing and treating pre-eclampsia. *Cochrane Database Syst Rev* 2000;(2):CD000492.