Review: Antiplatelet drugs reduce preeclampsia, preterm birth, and stillbirth or neonatal death

Duley L, Henderson-Smart D, Knight M, King J. **Antiplatelet drugs for prevention of pre-eclampsia and its consequences: systematic review.** BMJ. 2001 Feb 10;322:329-33. http://www.ahcpr.gov/clinic/evrptfiles.htm.

QUESTION

In pregnant women at risk for preeclampsia, how effective are antiplatelet drugs in preventing preeclampsia 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 to 1999) and by hand searching conference abstracts.

STUDY SELECTION

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

DATA EXTRACTION

Data were extracted on study validity (allocation concealment), patient risk for developing preeclampsia (high or moderate), length of gestation (< or ≥ 20 wk), dose of aspirin (≤ 75 mg or > 75 mg), whether the study was placebo-controlled, and outcomes (for women: preeclampsia, cesarean section, antepartum hemorrhage, serious maternal morbidity, and rare adverse events; for infants: death [stillbirth, neonatal, or infant], preterm birth [< 37 wk], 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 preeclampsia than did 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 cesarean 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 hemorrhage (8 trials), other neonatal bleeding (6 trials), or infant development (1 trial).

CONCLUSION

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

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Antiplatelet drugs vs placebo or no antiplatelet drug for women at risk for preeclampsia*

Outcomes at delivery	Number of trials	Weighted event rates		RRR (95% CI)	NNT (CI)
		Antiplatelet	Placebo		
Preeclampsia	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 preeclampsia, preterm birth, and their perinatal consequences among women at risk for preeclampsia. Small, randomized, 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 and colleagues have found that antiplatelet drugs confer important and statistically significant benefits on mothers at risk for preeclampsia 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 preeclampsia, 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 preeclampsia. The women most likely to benefit are those with a history of preeclampsia, chronic hypertension, or such medical problems as diabetes or renal disorders. Women with more moderate risk factors, however, may also benefit (e.g., first pregnancy, multiple pregnancy, family history of preeclampsia, teenaged mother, abnormal result on uterine artery Doppler scan or rollover test, or mild elevation in blood pressure without proteinuria). These women should also be offered this effective treatment.

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References

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2. **Knight M, Duley L, Henderson-Smart DJ, King JF.** Antiplatelet agents for preventing and treating pre-eclampsia. Cochrane Database Syst Rev. 2000;(2): CD000492.