South African National Essential Medicines List
Adult Hospital Level Medication Review Process
Component: Obstetrics

EVIDENCE SUMMARY:

Date: 3 February2020

Question: Is aspirin safe to use in pregnant women from 6 weeks gestation?

The recently published ASPIRIN trial[1] showed that low-dose aspirin – when taken between 6 weeks & 16 weeks gestation – significantly reduced perinatal mortality, fetal death, early preterm birth, as well as preterm delivery among pregnant women with hypertensive disorders.

This was a multinational, randomised, double-masked, placebo-controlled trial. Participants were recruited from seven community sites in six countries – India, Pakistan, Zambia, DRC, Guatemala & Kenya – between March 2016 and April 2019.

Women had to be between 6 weeks 0 days and 13 weeks 6 days pregnant at enrolment. Gestational age was confirmed by ultrasound. Participants were randomised to either aspirin or identical placebo. Study medication was taken until 37 weeks gestation or delivery. The participants were followed up every 2 weeks during pregnancy to assess adherence to medication. BP was assessed at 16-20 weeks, 28-30 weeks, 34 weeks, and then every 2 weeks until delivery.

The primary endpoint was the incidence of preterm birth (<37 weeks).
Secondary maternal outcomes included early preterm (<34 weeks) hypertensive disorders of pregnancy, vaginal bleeding, antepartum haemorrhage, postpartum haemorrhage, and maternal mortality.
Secondary predefined fetal/neonatal outcomes included fetal loss (16-20 weeks), perinatal mortality (stillbirths & early neonatal deaths after 20 weeks), early preterm birth (<34 weeks), small for gestational age (SGA), birthweight <2500g, birthweight <1500g, and miscarriage (<20 weeks).

11 976 women were randomised to either aspirin or placebo. Loss to follow up was 3.5%.
Adherence to study medication was high; 85.3% & 84.4% with aspirin & placebo, respectively.

Preterm delivery (<37 weeks) occurred in 11.6% in the aspirin arm vs 13.1% in the placebo arm: RR 0.89 (95% CI 0.81-0.98) p=0.012.
Early preterm delivery (34 weeks) also occurred less frequently with aspirin (0.1% vs 0.4%; RR 0.38 [95% CI 0.17-0.85]).

There were no significant differences between aspirin & placebo for adverse events – fetal loss (2.4% vs 2.7%), vaginal bleeding (0.2% vs 0.2%), and medical TOP/miscarriage (0.9% vs 0.9%).

Comments

The results of this study strengthen the findings of a 2007 Cochrane review[2] which showed that aspirin was associated with a 17% reduction in pre-eclampsia. In this review, early use of aspirin in pregnancy (before 20 weeks) was also not associated with a higher rate of fetal loss or placental abruption.

In yet another study (EAGeR)[3] published after this Cochrane review, 1 228 women with previous unexplained pregnancy losses, and planning a future pregnancy – were randomised to aspirin or placebo. In this trial aspirin was taken continuously pre-conceptually, throughout pregnancy, up to 36 weeks gestation or delivery.

Live birth rates were similar in the two groups (58% in the aspirin arm vs 53% in the placebo arm). Pregnancy loss occurred in 13% and 12% in the aspirin & placebo arms, respectively.

Vaginal bleeding early in pregnancy occurred more often with aspirin (40% vs 33%), but this did not translate into a higher rate of fetal loss. Birth defects were similar in the two groups (4 in each group).

The ASPIRIN study of nearly 12 000 participants provides further reassurance that aspirin use in early pregnancy is not associated with fetal loss, miscarriage, excessive vaginal bleeding, birth defects or medical TOP. Hence aspirin can be initiated as early as 6 weeks gestation.

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Conflicts of interest: Participated in development of NCCEMD National Guideline for gestational hypertension (SAMJ, 2019)

References

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