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Title: Effect of ASA on The Risk of Gestational Hypertension or IUGR and Prostanoid Synthesis in Pregnant Women Screened by Doppler Ultrasound

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## Abstract

The aim of the study was to evaluate the efficacy of low-dose ASA in the prevention of pregnancy-induced hypertension (PIH) and intrauterine growth restriction (IUGR) in high-risk pregnancies.

Within a dose range of 0.5-2.0mg/kg/day ASA had a favorable effect on the ratio of prostacyclin to thromboxane<sub>A2</sub> in hypertensive pregnancies. In the randomised, double blind and placebo-controlled trial 120 pregnant women considered to be at high risk of PIH or IUGR were screened by transvaginal Doppler ultrasound at 12-14 weeks of gestation. Ninety women with bilateral notches in the uterine arteries were randomised to ASA (0.5mg/kg/day) or placebo groups. Forty-three women in both groups were successfully followed up. The use of ASA was associated with a statistically significant reduction in the incidence of PIH (11.6% vs 37.2%, RR = 0.31, 95% CI 0.13-0.78) and pre-eclampsia (4.7% vs 23.3%, RR = 0.2, 95% CI 0.05-0.86). The incidence of hypertension before 37 weeks of pregnancy was also significantly reduced (2,3 % vs 20.9%, RR = 0.22, 95% CI 0.05-0.97). The reduction in the incidence of IUGR (2,3% vs 7%) was not statistically significant.

Bilateral notches in the uterine arteries at 12-14 weeks of gestation was a sensitive screening test (75-84%) in predicting hypertensive disorders of pregnancy but had rather low specificity (41-50%). The sensitivity of the test diminished with advancing pregnancy to 35% at 32-34 weeks of gestation and the specificity and positive predictive value increased to 94% and 59%, respectively.

Significantly lower prostacyclin at 12-14 weeks of gestation in the placebo group in pregnancies, which later developed pre-eclampsia, as compared to other pregnancies support the theory of endothelial dysfunction in pre-eclampsia occurring weeks before clinical disease is evident. Also pregnancies with bilateral notching had significantly higher  $9\alpha,11\beta$ -prostaglandin  $F_2$ , a vasoconstrictive metabolite of prostaglandin  $D_2$ , as compared to normotensive pregnancies at 12-14, and at 30-34 weeks of gestation.