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Maternal and Foetal Outcome With Low Dose Aspirin in Pregnancy Induced Hypertension

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Summary

The study was undertaken to find out whether low dose aspirin changes the maternal and foetal outcome. Of 76 patients, 40 received placebo and 36 received 50 mg of aspirin daily from the day of screening till 30 weeks of pregnancy. The development of hypertension was not affected by aspirin but cases with severe disease decreased in aspirin group. No statistical difference was found between duration of pregnancy, duration of labour and mode of delivery. There was slight increase in tendency of PPH (11% Vs 5%) but it was not statistically different. No case of APH was reported. Birth weight increased by 162 gm in aspirin group but it was not statistically significant. Apgar score was not different and there was no case of congenital anomaly, cephal haematoma or intraventricular haemorrhage. Prophylactic use of aspirin was not associated with a significant effect on the major pregnancy outcome.

Hypertensive disorders complicating pregnancy (PIH) are common and constitute a leading cause of maternal, fetal and neonatal mortality and hence attempt to prevent them appears to be justified. Primary prevention is only possible by avoiding pregnancy. Secondary prevention requires identification of patient at risk. Many studies have used low dose aspirin or calcium supplementation in high risk patients (Rogers et al ,1996) but the results are controversial. The Italian study recruited 13,486 pregnant subjects and used 50 mg/day aspirin without placebo and found no benefit in terms of prevention of PIH and perinatal mortality. American multicenter trials (Sibai et al, 1993) also found similar results. The randomised placebo controlled double blind study of 9,309 high risk pregnancies in Oxford (CLASP, 1994 Collaborative low dose aspirin study in pregnancy) gave 60 mg /day aspirin and there was no significant reduction in proteinuric PIH or perinatal mortality. However a greater proportion of pregnancies in aspirin treated group with early onset PIH continued beyond 37 weeks gestation. No excessive fetal abnormalities, haemorrhage risk or risk of abruptio placentae was reported for the treatment group. These data thus indicate that low dose aspirin should be reserved for specific 'high risk' pregnancies.

We studied the effect of 50 mg aspirin in the high risk group and evaluated the maternal and foetal outcome.

Material and Methods

The present study was carried out on the 421 patients who were screened for high risk pregnancy. Out of these, 396 patients could be followed till delivery. Patients were divided into two groups, low risk group comprising of 320 cases and high risk group comprising of 76 cases. Of 76 patients in high risk group, 36 were given 50 mg aspirin per day till 36 weeks of pregnancy while 40 patients were given placebo. The two groups

were matched for age, parity, family history of hypertension and past history of hypertension. The patients been especially assessed for development of hypertension, duration of pregnancy, duration of labour, mode of delivery and postpartum haemorrhage. The foetal outcome was seen in the form of birth weight, Apgar score and any congenital anomalies.

Results

There was no significant change in development of hypertension with use of aspirin. However the cases of severe PIH in aspirin group were only 5.5% vs 17.5% in placebo group. Only one patient in the placebo group had eclampsia (Table I). There was no significant change in duration of pregnancy or duration of labour in cases treated with aspirin and placebo . There was no significant change in mode of delivery though there was slight decrease in number of cesarean section from 32.5 to 27.5% in aspirin group. There was no significant change in incidence of PPH though aspirin group had 11.1% while placebo had 5% incidence of PPH. There was no case of antipartum hemorrhage in either group. Table II depicts the foetal outcome. There was no significant increase in birth weight by use of aspirin but the mean weight in aspirin users was more by 162 gm. There was no significant change in Apgar score. There were two intrauterine foetal deaths in placebo group while aspirin group had none. Congenital abnormalities, cephal haematoma, intraventricular haemorrhage or evidence of increased bleeding tendency was not seen in any case in either group.

Discussion

As pregnancy induced hypertension is a disease characterized by altered eicosanoid ratio, prophylactic aspirin therapy seemed a reasonable solution. Smaller doses of aspirin acetylate the cyclo-oxygenase in platelets within gastrointestinal capillaries of the pre-heptic circulation rendering them less aggregable and not enough concentration reaches the endothelium maintaining the PGI_2 production. Also smaller doses have less chance of any of the pharmacologically active drug reaching the uteroplacental circulation. Various studies have used different doses of aspirin. We have used 50 mg/day, same as used in Italian study of aspirin in pregnancy. In our study there was no significant difference in the outcome of disease in treated and non-treatment group. But the severity of disease was less in aspirin group (5.5% Vs. 17.5% incidence of severe pre-eclampsia).

CLASP (Collaborative low dose aspirin study in pregnancy) done in Oxford in 1994 on 9309 'high risk' pregnancies found no benefit in terms of significant reduction in proteinuric PIH, but some beneficial effect was seen in early onset disease. Though previous studies by Walsh (1985), Beaufils et al (1985) and Benigni et al (1989) showed reduction in risk of PIH and severe low birth weight. Sibai et al (1993) reported 4.6% incidence of pre-eclampsia whereas incidence of PIH was 6.7% and 5.9% respectively.

Table I. Maternal outcome

	Aspirin (36)	Placebo (40)
Hypertension		
Normotensive	28 (77.7%)	24 (60.0%)
Mild PIH	6 (16.6%)	8 (20.0%)
Severe PIH	2 (5.5%)	7 (17.5%)
Eclampsia	0	1 (2.5%)
Duration of pregnancy (months)	37.5 ± 1.94	37.25 ± 2.193
Duration of labour (hrs)	10.077 ± 2.38	11.44 ± 3.29
Mode of delivery		
Caesarean section	10 (27.7%)	13 (32.5%)
Vaginal delivery	26 (72.3%	27 (67.5%)
Postpartum haemorrhage		
Present	4 (11.11%)	2 (5.0%)
Absent	32 (88.8%)	38 (95%)

Table II. Foetal Outcome

	Aspirin (36)	Placebo (40)
Birth weight in kg.	2.717 ± 0.401	2.55 ± 0.5
Apgar score at 1 min	7.917 ± 0.692	7.375 ± 2.145
Apgar score at 5 min.	8.86 ± 0.723	8.57 ± 0.889

All studies have used different doses of aspirin, starting from different gestations and for different periods of time. Screening methods used were also different. As aspirin therapy is mainly a preventive treatment if started late it may not help much. Schiff et al. (1989) found similar decrease in proteinuric severe hypertension (2.9% Vs 22.6%) with 100 mg/day dose of aspirin in patients screened by roll-over test. This was explained by irreversible inhibition of platelet cyclo-oxygenase by aspirin causing correction in altered TXA_2 PGI_2 ratio in PIH.

No difference in duration of gestation was found in our study similar to studies of McParland et al (1990) and Benigni et al. (1989). Lewis and Shulman (1973) showed significant increase in duration of gestation and labour with 325 mg/day dose. As aspirin inhibits prostaglandin synthesis it may be anticipated that uterine contractions might be inhibited causing delay in onset and increase in length of labour. There was no increase in duration of labour in our study as low dose of drug does not inhibit prostaglandin synthesis markedly.

No significant difference in mode of delivery was found though there was some decrease in number of caesarean sections (27.7% vs 32.5%) similar to other studies (Sibai et al 1993; Schiff et al 1989).

The main concern with use of aspirin is regarding the predisposition to bleeding both in mother and fetus. There was no significant increase in risk of postpartum haemorrhage though it was increased from 5% to 11%. No case of antepartum haemorrhage was seen. This was in confirmation with findings of CLASP study (1994), McParland (1990) and Sibai et al (1993). Lewis and Schulman (1973) demonstrated increased blood loss at delivery but this was with high doses of aspirin. No cases of abruptio placentae occurred in our study unlike the increased incidence reported by Sibai et al. (1993). Our results were not confirmed by larger studies like Clasp (1994) where no increase in abruptio was found

Though there was increase in birth weight with use of aspirin by 162 gms it was not statistically significant. These results are consistent with those of Sibai et al and Italian study. McParland (1990) found increase of 155 gm but it was not significant. However, Wallenburg et al (1986) found significant reduction in number of growth retarded babies. Aspirin is used in cases of IUGR but is effective only if started early before irreversible vascular sclerosis has already occurred in the placenta (Trudinger et al, 1988).

Aspirin therapy did not affect Apgar score either at 1 min or after 5 minutes. One case of severe birth anoxia and two cases of intrauterine death were reported in non-treatment group. These results were not significant due to small sample size and findings were in agreement with those of other studies.

We did not find congenital anomaly in any baby in either group like other studies (Clasp 1994, Schiff et al 1989; Wallenberg et al 1986) Newborns in aspirin group did not show any increased evidence of bleeding, intraventricular haemorrhage or cephalhaematoma. Bleeding tendencies were reported in other studies (Sibai et al 1993, Clasp 1994, Benigni 1989) As we stopped the drug at 36 weeks in all patients no residual effect on coagulation profile was anticipated in the mother or the neonate. Though aspirin freely crosses placental barrier the low doses used by us usually do not affect neonatal platelet function. So prophylactic use of aspirin was not associated with a significant effect on the pregnancy outcome similar to the recent study by Bygruhanga et at (1998).

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