ROLE OF LOW DOSE ASPIRIN THERAPY IN THE PREVENTION OF PREGNANCY INDUCED HYPERTENSION

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SUMMARY

A prospective study was carried out to assess the role of low dose aspirin therapy in the prevention of pregnancy induced hypertension. The results showed that there was significant decrease in the incidence of severe PIH in the aspirin treated group as compared to the control group. Careful examination of the neonates revealed no bleeding tendencies or any congenital anomaly.

INTRODUCTION

Pregnancy induced hypertension occurs in upto 10% of pregnancies and may cause substantial maternal and fetal morbidity and mortality. The underlying cause remains unknown but most investigators agree that utero placental ischaemia plays an important role. Current knowledge implicates an imbalance between thromboxane and prostacyclin in the causation of utero placental ischaemia and thus PIH.

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Both thromboxane A_2 and prostacyclin (PGI_2) are derived from arachidonic acid through the action of the enzyme cyclo-oxygenase - Aspirin, by acetylating this enzyme may reduce the formation of both Thromboxane A_2 and PGI_2, but if given in low doses it can selectively suppress the synthesis of thromboxane A_2 without inhibiting the production of PGI_2 (Roth et al, 1975; Patrignani et al, 1982).

The present study has been undertaken to evaluate this peculiar property of low dose aspirin in PIH.

MATERIAL AND METHODS

Definition

Pregnancy induced hypertension was defined as systolic blood pressure in excess of 140 mmHg or diastolic blood pressure in excess of 90 mmHg or both, when measured on at least two occasions at least 24 hours apart, in women whose blood pressure had been previously normal. Severe pregnancy induced hypertension was defined as the development of

(a) Diastolic blood pressure in excess of 110 mm Hg or
(b) Persistent proteinuria of 2+ or more or 24 hour urinary protein excretion of 4 gm or
(c) Oliguria (urinary excretion less than 400 cc/24 hours or
(d) Convulsions

After ruling out diabetes mellitus, pre-existing hypertension and pre-existing renal disease, 80 patients at high risk for PIH (viz primigravida, patients with twin pregnancy and patients having previous history of PIH) and with positive roll over test were randomly divided into two groups of 40 each. Study group of 40 cases were given 75 mg Aspirin daily dispersed in a capsule starting from 28-30 weeks of gestation till 7 days before expected date of delivery. The other group serving as control were given capsule containing dextrose or other inert material.

Each patient was examined at fortnightly intervals. Fundal height, blood pressure and urinary protein levels were recorded at each visit. Patients who developed PIH were admitted. Their serum uric acid levels, blood urea, serum creatinine, fundus examination and ECG findings were recorded and they were managed in accordance with severity of the disease. The efficacy of low dose aspirin as a preventive measure against PIH was assessed by analysing the results statistically.

OBSERVATIONS

The study and control groups were well matched with respect to age, parity, rate of twin pregnancy and past obstetrical history.

With regard to the development of PIH the two groups were homogenous and did not differ significantly as shown in Table I. But most of the cases in the study group developed mild PIH while

Table 1

Development of PIH and Severe PIH

Characteristic	Study Group (n = 40)	Control Group (n = 40)	Statistical significance
PIH	16 (40%)	19 (47.5%)	P > 0.05 Not significant
Severe PIH	2 (12%)	12 (63.2%)	P < 0.05 Significant

those in the control group developed severe PIH.

As depicted in table II, in the control group, out of 9 cases in which forceps were applied, in 7 the indication was intrapartal fetal distress during the 2nd stage of labour. Also 2 patients underwent LSCS in the control group because of foetal distress. In the study group, intrapartal fetal distress occurred in only one patient and low forceps were applied.

Table III depicts the birth weight of infants in the study and control groups. With regard to birth weight, the two groups were homogenous and did not differ significantly at the 0.05 level of significance.

Careful examination of the neonates in the study and control groups revealed no bleeding tendencies or circulatory disorders or any other congenital malformation.

Table III

Birth Weight

Birth weight in Kg	Study group (n = 40)	Control group (n = 40)
Less than 2.5 kg	2	6
More than 2.5 kg	38	34

DISCUSSION

Roll over test proved to be an adequate and harmless screening test for the detection of those at a relatively high risk for pregnancy induced hypertension. 47.5% of the patients in the control group developed PIH. These results are comparable to those of Gusdon & Stephen (1977) who stated that in primigravida positive results predicted development of PIH in 50% cases.

In this study, the incidence of PIH did not differ significantly in the study and control groups. These results were similar to those of McParland et al (1990) and Benigni & Greonhii (1989). In contrast to the above studies Wallenburg et al (1986) and Schiff et al (1989) demonstrated a significant decrease in

Table II

Development of Intrapartal Fetal Distress and Mode of Delivery

Characteristic	Study Group (n = 40)	Control Group (n = 40)	Statistical significance
Intrapartal fetal distress	1	11	Significant
Normal vaginal delivery	38	34	Not significant
Application of forceps during vaginal delivery (Low or outlet forceps)	2	9	Not significant
Caesarean section	2	6	Not significant (P > 0.05)

the incidence of PIH in the Aspirin treated group.

There is a significant decrease in the incidence of severe PIH in the Aspirin treated group. These results were similar to those of Wallenburg et al (1986), Schiff et al (1989) and McParland et al (1990).

Intrapartal fetal distress for which low forceps application or LSCS had to be performed occurred in a significantly higher number of patients in the control group as compared to the study group. Schiff et al (1989) made similar observations. Thus it can be postulated that low dose Aspirin therapy improves utero placental circulation.

Careful examination of the neonates at birth revealed no abnormal bleeding tendencies. These observations are consistent with those of other prospective studies using aspirin less than 150 mg/day i.e. those conducted by Schiff et al (1989), Wallenburg et al (1988) and McParland et al (1990). Benigni & Greognii (1989) reported a decrease in 63% in fetal platelet cyclo-oxygenase after low dose aspirin therapy. These investigations were not done in the present study. Therefore, a small increase in risk for fetal bleeding tendencies even with low dose aspirin therapy cannot be ruled out.

To conclude, low dose aspirin therapy is safe and justified for the prevention of severe pregnancy induced hypertension in high risk patients. However, large studies are required to establish the optimum dosage schedule and the period of gestation at which it should be administered.

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