LOW DOSE ASPIRIN IN PREVENTION OF IUGR : A DOUBLE BLIND PROSPECTIVE RANDOMISED CASE CONTROLLED STUDY

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ABSTRACT

131 subjects were prospectively followed up on randomly dividing them into two groups. (A) Low lose aspirin group and (B) Placebo group. It was found that those subjects who were on low dose aspirin had a significantly decreased incidence of IUGR as compared to placebo. Also, these babies were heavier than placebo group. There was no difference in weight gain patterns of subjects in both the groups.

INTRODUCTION

Intra Uterine Growth Retardation or I.U.G.R. resulting from placental insufficiency has been in the focus of many a research. Due to many devastatingly bad complications being known to occur with it, methods to prevent it have always been looked for. Fitzgerald (1983) found that aspirin inhibits platelet adhesions to collagen under conditions of stasis or low flow. This important finding and subsequent research suggested a possible role of low dose aspirin in prevention of IUGR (Wallenberg - 1986).

In this carefully designed case controlled prospective double blind study, we have tried to study the effectivity of low dose aspirin in prevention of I.U.G.R.

SUBJECTS & METHODS

This prospective study was carried out in the Dept. of Obst. & Gynec., Medical College and S.S.G. Hospital, Baroda from 1st Jan. 1993 to 31st Dec. 1993. Mothers attending the antenatal OPD for antenatal care were screened and enrolled in this study on basis of following criteria :

(1) Primigravida

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(2) Singleton pregnancy

(3) Duration of pregnancy - Not more than 28 weeks and not less than 12 completed weeks of gestation.

All relevant data like age, relegion, parity and the like was recorded. Once enrolled these subjects were randomly grouped into aspirin and placebo group. Randomization was carefully done by its laid down rules and principles. As this was a double blind study, at the time of enrollment it was not known as to what drug the mother was given. Only the codes were known.

Low dose aspirin (75 mgms) was blinded against a placebo (100 mgms Lactose). They were made similar in appearance, size and colour by a local pharmaceutical company on request. These were then packed in identical packets and were then dispensed by one of the authors (MRD). These subjects who were enrolled, were instructed to take one tablet daily until 36 wks. of gestation.

They were then followed up at regular intervals. At each visit, the patient's weight, B.P. and urinary albumin examination were carried out. She was then subjected to a careful obstetric examination and all findings were meticulously noted. A routine ultrasonography was performed between 24-28 wks. and repeated if and whenever required. Fundal height, weight gain and USG were used to suspect I.U.G.R. antenatally and standard criteria (M. Singh - 1993) were used postnatally for confirming IUGR.

All subjects were followed upto delivery and obstetric outcome noted. At the end of the study, decoding was done and results analaysed and reviewed in the light of available literature.

RESULTS

In all 145 subjects were enrolled in this study. Of these 14 were lost to follow up for varied reasons. Thus, in all 131 cases could be followed up till the completion of delivery. There was a near equal distribution of these cases in both the groups. 65 in aspirin and 66 in placebo group.

All subjects were clearly instructed to discontinue the drug at 36 weeks of pregnancy. However one of the aspirin group continued taking the drug till delivery at 40 completed wks. No untoward effect was found in her.

Table I
Weight gain during pregnancy

Weight Gain	Placebo Group		Aspirin Group	
	No.	%	No.	%
Normal	52	78.78	52	79.99
More than normal	09	13.63	08	12.30
Less than normal	05	7.55	05	7.69
Total	65		66	

Maternal weight gain has long been considered as an indicator of IUGR. As shown in Table I, however no statistically significant difference was found in the weight gain of the subjects in both the groups. As regards normalcy of weight gain - 9-11 Kgms. of weight gain by term was considered as normal. Less than 9 Kgms. was considered as less than normal and more than 11 Kgms. was considered as more than normal weight gain.

As regards the neonatal outcome, only 12.31% had IUGR in the Aspirin group as compared to 30.3% in the placebo group. This difference was statistically significant (P< 0.001). Thus, aspirin group had less IUGRs than placebo group.

Birth weight of the newborns were also significantly different in both the groups, 7.69% of aspirin group had baby weight more than 3000 gms. the same being 3.03% in placebo group It was less than

Table II
Neonatal Outcome

Out come	Aspirin Group		Placebo Group	
	No.	%	No.	%
Fullterm-AFD	57	87.69	44	69.69
*Fullterm-SFD (IUGR)	08	12.31	20	30.31
Preterm - AFD	00	-	02	3.03
Preterm - SFD (IUGR)	00	-	00	-

*P < 0.001 : Statistically significant - AFD : Appropriate for date.
SFD : Small for date.

Table III
Birth Weight

Birth Weight (in gms.)	Aspirin Group		Placebo Group	
	No.	%	No.	%
More than 3000	05	7.69	02	3.03
2501 - 3000	52	80.00	43	65.15
2001 - 2500	08	12.31	16	24.24
1501 - 2000	00	-	04	6.06
Less than 1501	00	-	01	1.51

1500 gms. in 1.51% of placebo group whereas no such baby was found in the aspirin group. Also, 12.31% babies only were between 2001 to 2500 gms. in the aspirin group. The same figure was double 24.24% in the placebo group. Thus babies born to mothers on low dose aspirin were heavier than mothers on placebo.

DISCUSSION

In the present study it was found that I.U.G.R. occurred distinctly less frequently in babies born to those mothers who took low dose aspirin as compared to the placebo group. Wallenberg (1986) found in a nonrandomized trial that IUGR occurred in 61% subjects who were not taking aspirin as compared to 13% in subjects who were on aspirin. Similar results were shown by Hauth J. (1993) and Bochner H. (1986). Also, these workers as in the present study showed that babies born to mothers on aspirin were not only less growth retarded but were distinctly heavy in weight.

Thromboxane Az whether of placental or platelet in origin is a powerfull vasoconstrictor whereas prostacyclin of endothelial origin is a potent vasodilator. Low dose aspirin as shown by Vane (1971) selectively inhibits TXAz synthesis without affecting prostacyclin synthesis thereby improving the uteroplacetal flow. This could explain the successfull prevention of IUGR in subjects on low dose aspirin.

A healthy subject usually gains about 9-11 Kgms. of weight during pregnancy. The usual pattern being 1-2 kgms in 1st trimester and more or less linear rate of 0.4 kgms/wk. in the II & III trimester. A strong correlation is said to exist between maternal weight gain during pregnancy and the obstetric outcome. Menon (1991) showed that Indian women of low socioeconomic group gained about 6-7 kgms. during pregnancy. In the present study we did not find any significant difference in weight gain in mothers of aspirin group as compared to those in placebo group.

Williams (1993) mentions that the characteristic of preeclampsia is a sudden increase in weight. Though this may be indeed true, we did not find such a pattern in our study.

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