Original Articles

EFFECT OF MATERNAL LOW DOSE ASPIRIN ON NEONATAL PLATELET FUNCTION

Ranganna Dasari, Anil Narang, Kala Vasishta*, Gurjeevan Garewal**

From the Division of Neonatology, Department of Pediatrics and Departments of Obstetrics and Gynecology and Hematology**, Post Graduate Institute of Medical **Education** and Research, Chandigarh 160 012*

Reprint requests: Dr. Anil Narang, Additional Professor, Department of Pediatrics, PG1MER, Chandigarh 160 012.

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Objective: *To evaluate the effect of maternal low dose aspirin ingestion on platelet function of newborn* ***Design:*** *Prospective randomized placebo controlled study.* ***Methods:*** *25 neonates born to mothers receiving low dose aspirin and 25 matched neonates with no maternal exposure to aspirin were studied. 2 ml of EDTA and 4 5 ml of citrate blood was collected from umbilical vein using double clamped umbilical stump for hemogram, coagulation profile and platelet functions.* ***Results:*** *The platelet counts (W^{l}/1) of study and control groups were 186 4 ±22 76 (116-225) and 205 28 ± 17.34 (176-225), respectively. There was no significant difference in coagulation parameters. Prothrombin time index (PTI) was 86.24 ± 6.623 and 87 + 6.43, respectively in the study and control group while PTTK (sec) was 5588 ± 20 54 and 52 12 ± 11.82 in study and control subjects, respectively The platelet aggregation studies (platelet function) with various platelet agonists in study and control group did not show any significant difference. Clinically, none of the babies had bleeding.* ***Conclusion:*** *Use of low dose aspirin in pregnant women was found to be safe and had no adverse effects on platelet functions of newborn.*

Key words: *Coagulation, Maternal aspirin, Neonates, Platelet function.*

LOW dose aspirin is being used in pregnancy for prevention of pre-eclampsia and improvement of fetal growth in placental insufficiency(l-4). Aspirin is not an entirely safe drug, as it is known to inhibit platelet function even in low doses(5). *In vitro* testing demonstrated that newborns are much more susceptible to the effects of aspirin than adults(6). When aspirin is given to the mother, it is readily transferred to the fetus through placental barrier and may lead to mild to severe bleeding in the newborns(7-9). This study was carried out to evaluate the effects of prolonged low dose aspirin therapy on neonatal platelet function.

Subjects **and** Methods

Fifty primiparous women at 12 weeks gestation were randomly enrolled to receive aspirin or placebo (Lactic acid). Women with one or more complications were excluded from the study, chronic hypertension, any obstructive pulmonary disease, hypersensitivity to aspirin, history of peptic ulcer or hepatic disease, history of

long term treatment with nonsteroidal anti-inflammatory drugs (NSAIDS), diabetes melhtus, midtnmester abortion and antepartum hemorrhage Aspirin was used as 100 mg daily given till 36 weeks gestation Babies born to this cohort constituted the study subjects

Cord blood samples were taken for hematocrit, platelet count, PT, PTTK and platelet aggregation studies Platelet aggregation studies were performed in dual chamber chrono-log platelet aggregation using ADP, arachidonic acid, Ristocetin, collagen and epmephnne(10,ll)

Students 't' test and Chi-square test were used to evaluate statistical significance.

Results

The neonatal baseline characters and the laboratory parameters of both study and control group are summarized in *Table I* There was a significant difference in mean birth weight of babies in both groups ($p < 0\ 05$) As the study was mainly for term pregnancies and we could not control for birth weight and intrauterine growth, since, enrollment was on basis of antenatal administration of aspirin As mentioned in text, in the study group 92% were AGA and 4% SGA babies whereas in controls, 76% were AGA and 20% SGA babies None of the babies in study and controls required active resuscitation, their 1 minute apgar scores being 7 96 and 8 0, respectively None of the babies in both groups showed any evidence of bleeding manifestations at birth and during subsequent hospital stay There were no statistically significant differences in hemoglobin, rehculocyte count, the mean platelet count, and coagulation parameters (clot retraction, PT, PTI and PTTK) between the study and control groups ($p > 0\ 05$) *(Table II)*

The platelet aggregation response of study and control groups are summarized in *Table 111* There was no statistically significant difference observed in platelet

TABLE I - *Summary of Baseline Characteristics*

Parameter	Study group (Mean ± SD)	Control group (Mean ± SD)
Birth weight (kg)	2 .85 ± 0. 21*	2. 66 ± 0. 31
Gestation (wks)	38 .72 ± 0. 73	38 .6 + 1. 28
Mode of delivery		
NVD	17 (68%)	18 (72%)
Instrumental	6 (24%)	2 (8%)
LSCS	2 (8%)	5 (20%)
No. of cases requiring active resuscitation	Nil	Nil
Apgar score		
1 min	7 .96 ± 0 . 2	8.0 + 0.0
5 min	9 .88 ± 0 .33	9 .96 ± 0. 2

Except * ($p < 0\ .05$), none of the differences between the two groups were significant
NVD = Normal vaginal delivery
LSCS = Lower segment Caesarean section

TABLE II - *Hemogram Values of Study and Control Groups*

Laboratory parameter	Study group (n = 25)	Control group (n = 25)
Clot retraction (%)	65.04 (42-75)	65.0 (55-76)
Prothrombin time index (PTI) (sec)	86.24 ± 6.62	87.47 ± 6.43
Partial thromboplastin time with Kaolin ratio (PTTKR) (sec)	1.54 ±0.23	1.48±0.17
Platelets (1071)	186.40 ± 22.76 (116-225)	205.28 ± 17.34 (176-225)

None of the differences between the two groups were significant.
Figures in parentheses indicate the range.

TABLE III - *Platelet Aggregation Responses of Study and Control Groups*

Group	ADP		Arachidonic acid		Ristocetin		Collagen		Epinephrine	
	Resp	Not Resp	Resp	Not Resp	Resp	Not Resp	Resp	Not Resp	Resp	Not Resp
Study group	23	2	23	2	21	4	0	25	0	25
Control group	25	0	24	1	23	2	0	25	0	25

Resp = Responded

aggregation studies with various platelet agonists (ADP, Arachidonic acid and Ristocetin). In both the study and control groups platelet aggregation did not show response to epinephrine and collagen. The maximum platelet aggregation (peak) with ADP in study and control groups were 51.02% ± 20.90 and 56.02% ± 18.16, respectively.

The mean slope (cm/min) H with ADP of study and control were 10.36 ± 3.81 and 9.64 ± 3.33, respectively. The mean difference of peak and slope with ADP was not significant ($p > 0.05$). The maximum (peak) response with arachidonic acid in study and controls were 69.15% ± 12.19 and 69.82% ± 12.37, respectively. The mean slope (cm/min) with arachidonic acid of study and controls were 13.39 ± 4.86 and 11.99 ± 3.56, respectively. The mean difference of peak and slope with the arachidonic acid was not significant statistically ($p > 0.05$). The mean maximum (peak) response with ristocetin in study and controls were 67.52(%) + 15.19 and 69.77(%) ± 12.94, respectively. The mean difference of peak and slope with ristocetin was not significant statistically ($p > 0.05$).

Discussion

The use of low dose aspirin has been proposed for the prevention of pre-eclampsia and intrauterine growth retardation(12,13). Aspirin acts via the irreversible acetylation of the platelet enzyme cyclo-oxygenase which is responsible for synthesis of thromboxane A_2 (TXA_2), which is a potent vasoconstrictor and promoter of

platelet aggregation(9). As aspirin rapidly crosses the placenta, it is possible that the use of aspirin may result in neonatal morbidity secondary to impaired neonatal platelet reactivity and altered prostaglandin synthesis(14).

In our study, aspirin given to the mother apparently helped in weight gain without causing any clinical bleeding manifestations^). Neonates were followed up for any evidence of bleeding manifestations upto 3 days or till hospitalization. The study had envisaged evaluation of coagulation profile and antenatal exposure of aspirin. The beneficial effects of *in utero* exposure in improving birth weight of babies have also been documented by others(l,15-17). These findings are similar to those reported in earlier studies(l,2,4,18,19). No statistically significant difference was observed in platelet aggregation studies with variou,s platelet agonists (ADP, Arachidonic acid, Ristocetin) either in the mean maximal response or the mean slope.

In the study group out of the 25 neonates, 8 did not show platelet aggregation response to physiological agonists (2-ADP, 1-AA, 4-Risto), whereas in case of controls, 3 of them did not show a response (O-ADP, 1-AA, 2-Risto). This type of non response has also been documented in earlier studies of platelet function in normal neonates(20-23). These studies proposed that a defect could be in the sensitivity and structure of the receptor to ADP, and also defective Ca^{++} release after receptor-agonist interaction and the "storage pool" may contain less amount of ATP and ADP in neonatal platelets.

In conclusion, maternal low dose aspirin therapy used for prevention of preeclampsia and decreasing the incidence of IUGR is not associated with any observable neonatal effects in the form of increased bleeding tendencies. There was also no associated platelet dysfunction nor any disturbances in the hematological or coagulation parameters in the neonates.

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