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Role of Low Dose Aspirin in Mothers Registering High Serum HCG Levels at Mid Trimester

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Summary

HCG has an important role in predicting immunological conditions like pre-eclampsia remote from term as has been proved by a series of studies. As a natural consequence of this, a clinician would always like to know if after predicting these conditions, they can be prevented by any means or atleast their fury ameliorated. In this prospective study we have tried to explore the possibility of low dose aspirin in influencing the progress and outcome of these conditions. Subjects with past history of recurrent missed abortions, intra uterine growth retardation, unexplained still births, pre eclampsia and/or eclampsia remote from term, deep vein thrombosis in last pregnancy or chorea gravidarum who had βHCG > 2M.O.M. at midtrimester this time were included in this study. every alternate one were given aspirin in a dose of 1.2 mg/kgm/day. Full term delivery was significantly more in the group in whom aspirin was given. Preterm delivery however did not have any significant difference. Spontaneous abortions were indeed less in cases where aspirin was given. Pre-eclampsia remote from term and IUGR were significantly less in the aspirin group. Birth weights of the babies born to mothers in whom aspirin was given increased to a point but not beyond.

Introduction

There were two interesting developments in the dying decades of the last millennium that have added new depth to our understanding of some high-risk obstetric conditions. These are establishment of an irrefutable association between pre-eclampsia remote from term, recurrent missed abortions, etc and antiphospholipid antibody syndrome and 2) of the immunological face of HCG (Caruso et al 1999). These two developments in obstetric immunology had profound bearings. It was also conveyed through a series of studies that HCG might have an important role in predicting immunological conditions like pre-eclampsia remote from term (Lambert-Messerlian et al, 2000. Onderoglu and Kabukcu et al, 1997). Yaron et al (1997) showed that β-HCG was found to be associated with poor pregnancy outcome : including intrauterine growth restriction (19%), pregnancy-induced hypertension (14%), and preterm labor (19%). As a natural consequence of this, a clinician would always like to know if after predicting these conditions they can be prevented or atleast their fury ameliorated.

In this prospective study we have tried to explore the possibility of low dose aspirin in influencing the progress and outcome of these conditions.

Materials and Methods

This study was carried out over a period of a little over 5 years from 1st Jan. 1996 to 31st Jan. 2001. Subjects with past history of recurrent missed abortions, intrauterine growth retardation, unexplained still births, preeclampsia and /or eclampsia remote from term, deep vein thrombosis in last pregnancy or chorea gravidarum were included in this study. These mothers were subjected to serum βHCG level testing at around 15-16

weeks of this pregnancy. βHCG levels greater than 2 M.O.M. for that week of gestation were considered high.

Every alternate subject were given aspirin in a dose of 1.2 mg/kgm/day as soon as the report was received. The remaining formed control. Both groups were similarly followed up for their obstetric outcome.

The results so obtained were checked for their significance using standard students' chi-square test and these were counter checked on SPSS software.

Results

In this period of 5 years, 215 cases were included in the study. But 38 were those who were either lost to follow up or were dropped from analysis as their records were found to be incomplete. In all there were 178 cases that could be included in the study for final analysis. Of these 178, 88 subjects were in the aspirin group (Group A) and 90 were in non-aspirin group (Group-B).

It is obvious from this Table I full term delivery was significantly more in the group in whom aspirin was given. Preterm deliverers however did not have any significant difference. Spontaneous abortions were indeed less in cases where aspirin was given. But on application of statistical indices in this outcome, it barely reached levels of significance (P<0.02 at df 1). However it should be remembered that estimation of HCG was done at 15-16 weeks. By this time most of the abortions if destined to occur, must have occurred. Also, the drug was started at 15-16 weeks and the period of abortion is considered only upto 20 weeks. So while analyzing the result for the effect on spontaneous abortions this vital aspect must be considered.

Table II analyzes the effect of the drug on two conditions with immunological basis: Pre-eclampsia remote from term and IUGR. In both these conditions the beneficial effect of the drug was highly significant (P<0.001).

One more area where the effect of drug was studied was on birth weights. It was found that significantly more babies (P<0.001) had birth weights less than 2.5 kgms when aspirin was not given. It seems that more babies in the weight group of 2.5 to 3 kgms. were born in mothers where aspirin was given, the difference just managing to reach the levels of statistical significance (P<0.02). But there was no significant difference in babies born in weight group of more than 3

Table I
Obstetric Outcome

	Group A (N=88)		Group B (N=90)		X^2	P-value
	No.	%	No.	%		
Full term delivery	71	80.7	54	60	9.1	< 0.01
Preterm delivery	11	12.5	19	21.1	2.32	< 0.05
Spont. Abortions	06	6.8	17	18.9	5.31	< 0.02

Group A: N=88 – cases where aspirin was given
Group B: N=90 – cases where aspirin was not given

Table II

	Group A	%	Group B	%	X^2	P-value
Preeclampsia remote						
From term	21	23.9	55	61.1	39.45	< 0.001
IUGR	06	6.8	37	41.1	28.72	< 0.001

Group A: N=88 – cases where aspirin was given
Group B: N=90 – cases where aspirin was not given

Table III
Birth Weight

	Group A		Group B		X^2	P-value
	No.	%	No.	%		
> 3 kgms	23	26.1	14	15.6	3.01	< 0.05
2.5 to 3 kgms	53	60.2	35	38.9	5.09	< 0.02
< 2.5 kgms	12	13.6	41	45.6	29.8	< 0.001

Group A: N=88 – cases where aspirin was given
Group B: N=90 – cases where aspirin was not given

kgms. (Table III). Thus birth weights of the babies born to mothers in whom aspirin was given, did increase to a point and not beyond.

Discussion

The results of this study are an attempt to apply immunology in clinical practice. It is known through a series of studies that in obstetric conditions with immunological bearing elevation of the βHCG levels in the second trimester of pregnancy is an indication for extra vigilance during further prenatal care (Bahado-Singh et al 2000. Heinonen et al 1999, Morsink et al 1995). Liu et al (1999) conclusively proved the immunological application of HCG when they demonstrated that patients with elevated maternal serum HCG showed an increased volume of HCG-positive trophoblast per unit surface area and increased intensity of HCG immunoreactivity within individual terminal villous units. HCG levels estimated at mid-trimester have a vital role to play in predicting these. But to a clinician the cardinal question is can one prevent the adverse outcome, once predicted? It is suggested that treatment strategies for the prevention of adverse obstetric outcome in these conditions be warranted because treatment appears to alter fetal outcome favorably (Corusu et al, 1997). This is where role of aspirin requires to be investigated.

The rationale for using aspirin in these cases emanates from the all-famous CLASP study. While denying any significant role for aspirin in preventing PIH the same study does underline its role in pre-eclampsia remote from term. This type of PIH has immunological basis. It is therefore logical to expect a role of aspirin in allied immunological conditions, as well. With this rationale the present study was prospectively undertaken. Also Viinikka et al (1993) strongly suggested the role of aspirin in improving the feto-maternal vascular interface.

Full term delivery was significantly more in cases where aspirin was given but there was no difference in preterm deliveries. Abortions were less in the group where aspirin was given. As has been mentioned in analysis section, this HCG estimation has been done at around 15-16 weeks. This leaves a mere four weeks latitude for documenting an abortion. In spite of a short period of one month the difference did manage to reach the level of significance albeit barely.

Wenstrom (1998) conclusively proved that the birth weight of children born to mothers who were given aspirin following high β-HCG at 15-16 weeks, increased. In the present study overall birth weight of babies did increase after administration of aspirin in mothers with high βHCG albeit to a particular point. This difference was most distinct in the group with birth weight less than 2.5 kgms. There was an increase in birth weight but not beyond 3 kgms. This should be viewed from the fact that this study is carried out in public hospitals where the mean birth weight is around 2.5 kgms. It is not very common to find babies with birth weight greater than 3 kgms. This shows the inherent potential of these mothers to give birth to babies of about 2.5 kgms. This inherent potential has got manifested here. As a result the birth weight increased only upto a particular point and not beyond.

It also shows an allied aspect. Spong et al (1998) have shown that raised HCG levels are a result of defective angiogenesis. Administration of aspirin restores a state of normalcy in the feto-placental interface effectively reversing this vasculopathy generated in immunological conditions. Obviously it is not a drug that promotes weight of the fetus. Obstetric conditions like recurrent missed abortions, IUGR, stillbirth, pre-eclampsia are known to have an immunological basis. Administration of low dose aspirin in these cases can prevent the adverse outcome albeit to some extent.

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