PLATELETS AND FIBRINOLYTIC ACTIVITY IN PRE-ECLAMPSIA AND ECLAMPSIA

By

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SUMMARY

In patients of pre-eclampsia and eclampsia there was mild to moderate depression of FLA and platelet counts compared to normal pregnancy. The return to normal was also slow in cases of severe pre-eclampsia and eclampsia as values estimated 48 hours post-partum were still high. The platelet lifespan and thromboxane A_2 remained almost unaltered during the course of normal pregnancy. In patients of severe pre-eclampsia, the platelet life-span was significantly shorter than that of mild and moderate pre-eclampsia. Similarly, thromboxane A_2 levels were significantly higher in cases of severe pre-eclampsia and eclampsia as compared to normal pregnancy. Overall the results of this study provide evidence to support the hypothesis that an abnormality in the fibrinolytic system, platelet life-span and thromboxane A_2 levels are related to pre-eclampsia and eclampsia.

Introduction

The occurence of infarction in placenta of pathological pregnancies is a well known fact. Studies on fibrinolytic system in pre-eclampsia have provided conflicting results. Bonnar *et al* (1971) and Howie *et al* (1971) demonstrated changes in the coagulation and fibrinolytic system in severe pre-eclampsia consistent with the view that intravascular coagulation is present in this syndrome, while Gaw *et al* (1984) reported no difference in the mean levels of fibrinolytic activity and inhibitory activity against urokinase and tissue activator in these cases when compared to uncomplicated pregnancies. The present study was performed to find out the fibrinolytic activity, platelet life span and thromboxane A_2 synthesis in pre-eclamptic and eclamptic pregnancies in comparison to normal pregnancies.

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Material and Methods

The study was carried out on 20 normal non-pregnant women in the reproductive age-group who served as control, 93 cases of normal pregnancy, 10 of pre-eclampsia and 13 of eclampsia. Some of these cases were followed post-partum. In all these cases estimation of platelet count was done by using Rees-Ecker diluting fluid (Wintrobe, 1967) and later confirmed by

slide method (Sonnewirth anl Jarett, 1980); estimation of fibrinolytic activity (FLA) was done by measuring (a) euglobulin clot lysis time (ECLT) (Buckwell, 1958) and (b) Whole blood-clot lysis time (Cartwright, 1963); platelet life-span was measured by a non-radioisotopic technique (Stuart *et al* 1975), and thromboxane A_2 (Tx A_2) synthesis was estimated by the method of Best *et al* 1980.

Results

The value of FLA by method of ECLT (Table I) in three trimesters indicated a gradual fall in the FLA with advance of pregnancy, which returned towards normal 48 hours after delivery. The mean values of ECLT in the toxamia of pregnancy also showed a decrease in FLA according to the severity of the disease. FLA estimated 48 hours postpartum was not found to be significantly different from the antepartum values, indicating that the return of FLA to normal after delivery was very slow.

The values of whole blood clot lysis time (WBCLT) are shown in Table II. Ninety five per cent of non-pregnant women showed clot-lysis within normal range of 48-72 hours and only in 5% cases WBCLT was greater than 72 hours. In pregnant patients, 6.45%, 12.12% and 13.79% cases showed WBCLT more than 72 hours in the three trimesters of pregnancy respectively. In 20% patients with mild to moderate pre-eclampsia it was seen to exceed 72 hours. In patients of severe pre-eclampsia and eclampsia 33.33 and 30.77% of patients respectively showed clot lysis time of greater than 72 hours.

Platelet counts (Table I) like FLA also showed a gradual fall with advancing period of gestation. The post-partum value showed a return towards the normal 48 hours after delivery. Platelet count was significantly decreased in patients of severe pre-eclampsia and eclampsia compared to normal pregnancy.

The platelet life-span (Table I) was measured by non-radioisotopic technique. There was no significant difference in platelet life-span between non-pregnant and pregnant women. In patients of severe pre-eclamsia the platelet life-span was significantly shorter than in mild and moderate pre-eclampsia and in normal pregnant and non-pregnant women.

Thromboxane A_2 levels (Table I) were found to remain unaltered during the course of normal pregnancy. Its value in severe pre-eclampsia and eclampsia were significantly higher than in normal pregnancy.

Discussion

The present study confirms that there are considerable differences in tests of fibrinolysis and platelet function between normal pregnant patients and those with severe pre-eclampsia and eclampsia. The FLA was found to be decreased significantly ($P < 0.05$) in severe pre-eclampsia and eclampsia when compared to normal pregnancy. Reduced FLA in toxaemia has also been reported by some workers in the past (Bonnar *et al*, 1969 and 1971 and Birmingham Eclampsia Study Group, 1971). The decrease was cited to be due to decreased levels of circulating plasminogen activator.

The platelet counts were significantly lower in severe pre-eclampsia and eclampsia ($P < 0.01$) compared to normal pregnancy. However, in cases of mild and moderate severity the difference was not statistically significant ($P > 0.60$). Neilson (1969), Howie *et al* (1971) and Dube

TABLE I

Comparison of FLA, Platelet Count, Platelet Life Span and TxA_2 in Pregnant, Non-pregnant, Post/Partum, Pre-eclampsia and Eclampsia Patients

Diagnosis	No. of cases	ECLT (in minutes)		Platelet count (in lacs/mm³)		Platelet Life span (in days)		TxA^2 (in n moles/ 109 Platelets	
		Mean ±S.D.	p value	Mean ±S.D.	p value	Mean ±S.D.	p value	Mean ±S.D.	p value
Non-pregnant	20	171.0 ±12.31	—	3.089 ±0.417	—	9.1 ±0.54	—	5.05 ±0.68	—
Pregnant									
I Trimester	31	159.03 ±39.54	>0.10	2.940 ±0.360	>0.20	8.84 ±1.08	—	5.08 ±0.75	—
II Trimester	33	276.67 ±51.85	<0.001	2.640 ±0.161	<0.001	8.76 ±0.922	—	5.22 ±0.944	—
III Trimester	29	357.76 ±63.78	<0.001	2.417 ±0.169	<0.001	8.724 ±0.867	—	5.23 ±0.887	—
Post partum	21	288.09 ±14.01	<0.001	2.611 ±0.149	<0.001	— 8.2	—	—	—
Pre-eclampsia: Mild & Moderate (Ante partum)	10	343.0 ±43.83	>0.05	2.388 ±0.199	>0.60	±0.748	>0.05	5.35 ±0.564	>0.06
Severe (Ante partum)	6	413.33 ±22.85	<0.05	2.167 ±0.075	<0.001	7.66 ±0.745	<0.02	6.21 ±0.600	<0.02
Post-partum	6	350.0 ±50.0		2.03 ±0.140	—	—	—	—	—
Eclampsia	13	402.69 ±29.46	<0.05	2.173 ±0.230	<0.01	Could not be estimated		6.06 ±0.519	<0.01
Ante partum									
Post partum	6	381.67 ±42.98	—	3.22 ±0.103	—	—	—	—	—

TABLE II

FLA as Determined by Whole Blood Clot Lysis Time (WBCLT) in Hours in Non-pregnant, Normal Pregnant, Post Partum, Pre-eclampsia and Eclampsia Patients

Diagnosis	No. of cases	0-24 Hrs.		24-48 Hrs.		48-78 Hrs.		72 Hrs.	
		No. of cases	Per cent	No. of cases	Per cent	No. of cases	Per cent	No. of cases	Per cent
Normal Nonpregnant	20	—	—	—	—	19	95.0	1	5.0
Normal Pregnancy:									
1st Trimester	31	—	—	—	—	29	99.55	2	6.45
2nd Trimester	33	—	—	—	—	29	87.88	4	12.12
3rd Trimester	29	—	—	—	—	25	86.21	5	13.79
48 Hours Postpartum	21	—	—	—	—	20	95.24	1	4.76
Abnormal Pregnancy:									
Pre-eclampsia	10	—	—	—	—	8	80.0	2	20.0
Severe pre-eclampsia	6	—	—	—	—	4	66.67	2	33.33
Eclampsia	13	—	—	—	—	9	69.23	4	30.77

et al (1975) also reported decreased platelet count in their studies. Low grade intravascular coagulation was implicated to be the cause of decreased platelet count. However Whigham *et al* (1978) attributed the decrease to platelet consumption in microcirculation of organs such as placenta, kidney and liver.

Platelet life-span was not different in normal pregnant women when compared to the non-pregnant women. Similar findings have been reported in the past (Wallenburg and Van Kessel, 1978 and Rackoczi *et al*, 1979). This would seem to indicate that either the quantity of platelet consumption is not much or that new platelets are easily able to replace the consumed ones.

The decrease in platelet life-span in patients of severe pre-eclampsia was significant ($P < 0.05$) whereas the difference was not significant in patients of mild to moderate pre-eclampsia ($P > 0.05$). Similar observations have been reported by Rackoczi *et al* (1979). Abnormal placental endothelium in severely pre-eclamptic patients is known to cause platelet consumption, which leads to shortened platelet life-span. Harken and Slichter (1974) were of the view that an abnormal endothelial surface is responsible for an increased local consumption of platelets.

The value of TxA_2 in the three trimesters of normal pregnancy were not different from those obtained in non-pregnant women ($P > 0.50$). Pregnancies complicated with severe pre-eclampsia and eclampsia showed a significantly higher production of TxA_2 ($P < 0.05$), but it was not so in patients of mild and moderate pre-eclampsia. Increased reactivity of platelet TxA_2 pathway due to decreased platelet cyclic adenosine monophosphate (cAMP) may be a contributing

factor. The decreased level of cAMP in turn results from decreased production of vascular PGI_2 in these subjects (Ferguson *et al* 1975). The increased production of TxA_2 in pre-eclampsia has been reported by Remuzzi *et al* (1980).

Taken together, the changes in fibrinolysis and platelets support the hypothesis that intravascular coagulation is occuring in severe pre-eclampsia and eclampsia. The findings further support the hypothesis of a disturbed prostacyclin-thromboxane A_2 balance in the uteroplacental vascular bed, leading to an increased tendency of platelets to aggregate with formation of occlusive thrombi and hence uteroplacental insufficiency.

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