A Study of the of Role Platelet and Fibrinolytic Activity in Pathophysiological Changes in Pre-Eclampsia

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Abstract : *Eight severe pre-eclampsia, 21 mild pre-eclampsia and 12 normal pregnancies were selected from the antenatal care unit of Siriraj Hospital to study their platelet aggregation and fibrinolytic activity both during pregnancy (>20 weeks gestation) and after delivery. It was found that platelets of normal pregnant subjects and both groups of pre-eclamptic patients were hypersensitive to collagen, adrenaline and ADP. After delivery, only normal pregnancy revealed singificant decrease in percent maximal aggregation ($p<0.05$) while pre-eclampsia did not show any significant difference. This may be due to the enhancement of gestational effect on platelet activity which returned to normal after delivery. However, hyperactivity of pre-eclamptic patients may not only be due to the gestational effect alone, but also to the original hyperactive activity of platelet. before pregnancy. Fibrinolytic activity was also found to be decreased significantly in pre-eclampsia because euglobulin lysis time was prolonged over the normal ranges but after delivery it returned to normal. (Thai J Obstet Gynaecol 1993;5: 57-62.)*

Key words : platelet, fibrirolytic activity, pathological changes, pre-eclampsia

In general, pre-eclampsia (PE) is progressively developed to eclampsia which is a major cause of foetal and maternal norbidity and mortality and is often associated with foetal growth retardation. The aetiologies of this disease are still not completely understood, more than one mechanism probably contributes to it. Platelets have been implicated in one of the complex aetiologies of this condition[1] because there is evidence from a number of studies which indicates that anti-platelet therapy given early in high risk pregnancy may protect against PE[2,3]. The alteration in platelet function has been recognized as the important feature of this pathology[4-6] because they may be involved in the formation of microthrombi in the utero-placental circulation which possibly initiates the complication during pregnancy.

Fibrinolytic activity is another

factor which may be involved as aetiopathogenesis of PE. It has been established that fibrinolysis is diminished throughout pregnancy[7,8]. Hypofibrinolysis is also found in PE[9]. This study is, then, designed to determine the degree of platelet aggregation and fibrinolytic activity in the same pre-eclamptic patients compared with the same normal pregnant women, both during pregnancy and after delivery. It is believed that knowledge gained from this study will eventually be of benefit for establishing an approach for early detection and early management of PE.

Materials and Methods

Subjects

Pre-eclamptic patients and normal pregnant subjects were screened by the obstetrician from admitted patients and from the antenatal care unit of Siriraj Hospital.

Pre-eclamptic patients were pregnant subjects who developed hypertension after 20 weeks of gestation, on at least 2 separate occasions, with edema and/or proteinuria. Mild PE is defined as mild hypertension (diastolic blood pressure between 90-100 mmHg) with edema and/or proteinuria (1^+-2^+). Severe PE is defined as severe hypertension (diastolic blood pressure>100 mmHg) with edema and/or proteinuria (>2^+). Normal pregnant subjects were normotensive pregnant subjects whose age and gestational age were compatible with the selected mild and severe pre-eclamptic subjects.

Exclusion criteria were patients/subjects who had taken NSAIDs or any drugs known to effect either platelets or prostaglandin synthesis, during 2 weeks before the study or having a history of hypertension before their pregnancy or having suspected renal disease or having diabetes mellitus.

Specimen collection

Venous blood of each subject was collected twice, during pregnancy and after delivery (48 hours). Platelet aggregation was measured by the optical technique[10]. The concentrations of platelets in platelet rich plasma were in the range of 3.00 - 4.00 X 10^8/ml. Fibrinolytic activity was determined as euglobulin lysis times (ELT).

Statistical analysis

Kruskal-Wallis test or Wilcoxon Matched-Pair Signed Rank test was employed to test the differences of variables among/or within subject groups.

Results

The clinical characteristics of the studied subjects are shown in Table 1. During pregnancy, subjects possessing hyper-aggregation platelets were frequently found in all 3 groups

Table 1 Characteristics of studied groups

Characteristics	NP	Mild PE	Severe PE
No. of subjects	12	21	8
Age (yrs.)	22 ± 4	24 ± 6	25 ± 9
Gestational age (wks.)	28 ± 5	36 ± 3	38 ± 3
Blood pressure :			
Systolic (mmHg)	112 ± 10	137 ± 16	156 ± 11
Diastolic (mmHg)	72 ± 8	92 ± 12	108 ± 7
Proteinuria			
(No.of positive subjects)	-	4	8
Edema			
(No.of positive subjects)	-	21	8
Parity :			
Nulliparous	11	14	5
Multiparous	1	7	3
Birth weight (kg)	3208 ± 333	2604 ± 687	1980 ± 730

Table 2 Platelet aggregation patterns in NP and PE

Pattern of platelet aggregation	NP		Mild PE		Severe PE	
	ante-partum	post-partum	ante-partum	post-partum	ante-partum	post-partum
Hyper-	9	8	17	16	6	6
Normal-	2	4	4	4	2	1
Dis-	1	0	0	1	0	1
Total	12		21		8	

Table 3 Percent maximal aggregation of platelets in NP and PE

Maximal aggregation induced by	NP		Mild PE		Severe PE	
	ante-partum	post-partum	ante-partum	post-partum	ante-partum	post-partum
Collagen	62.3 ± 21.4	54.5 ± 8.7	57.2 ± 14.6	51.2 ± 16.1	58.0 ± 11.5	43.3 ± 25.0
Adrenaline	46.7 ± 26.6	18.5 * ± 16.6	43.8 ± 22.3	33.1 ± 21.5	34.0 ± 29.1	38.5 ± 26.2
ADP	61.8 ± 16.3	35.6 * ± 20.6	54.9 ± 17.9	53.5 ± 15.2	43.3 ± 23.4	47.2 ± 24.9
Platelet ($x10^8$/ml)	3.59 ± 0.54	3.66 ± 0.69	3.00 ± 0.68	3.03 ± 1.03	3.16 ± 1.13	3.61 ± 1.23

* $p<0.05$

Table 4 Fibrinolytic activity (euglobulin lysis times) in NP and PE

	NP	Mile PE	Severe PE
Antepartum	267 ± 73	304 ± 66	308 ± 59
Postpartum	227 ± 89	244 ± 75*	254 ± 89

* $p<0.05$ (Normal range<300 minutes)

while subjects possessing dis- or normal-aggregation platelets were less common. In qualitative measurement it was found that after delivery, the number of subjects possessing hyper-aggregation platelets in NP and in mild PE were slightly decreased while there was no change in severe PE (Table 2).

In quantitative measurement, the percent maximal aggregation of platelets after being induced by collagen, adrenaline or ADP in each subject group were averaged and tabulated in Table 3. During pregnancy, there was no significant difference in the percent maximal aggregation between these 3 groups. After delivery, the percent maximal aggregation was decreased significantly in normal group ($p<0.05$) while they did not significantly change in the pre-eclamptic groups ($p<0.05$).

Fibrinolytic activity was expressed as ELT. During pregnancy ELT of NP, mild and severe PE, were not significantly different. After delivery ELT of mild PE was significantly decreased (Table 4).

Discussion

It was found that most of the subjects had hyperactive platelets. In our data collected, hyperactive platelets were found in only 30% of non-pregnant women. It is possible that platelets may be enhanced by gestational effect to be hyperactive during pregnancy then usually return to normal after delivery[11]. However, in this study only maximal aggregation of NP was significantly reduced after delivery while PE was not changed. It might be questioned whether their platelet aggregation showed hyperactivity before pregnancy then initiated PE or PE developed first then hyperactivity followed. The hyperactive platelets might be an important risk factor for the pathogenesis of PE through their involvement in the formation of micro-thrombi in the utero-placental circulation because it has been reported that thrombi were found in the small blood vessels of patients dying after eclampsia[12]. The concept that subjects with hyperaggregation platelets have a higher risk for developing PE is confirmed by the review of Halushka et al[13] who concluded that diabetic pregnancy had an increased incidence of pregnancy-induced hypertension. Moreover, it has been long known that platelets

of diabetic patients are hyperactive[14].

The study on fibrinolysis of NP and PE revealed that there was some impairment in fibrinolytic activi ty of these patients during pregnancy because their ELT was found not only last longer than ELT after delivery but also prolonged over the normal range. Impairment in fibrinolysis may be associated with fibrin deposition in the vessels of pre-eclamptic patients. By using immunofluorescent method, Vassalli et al[15] and Hustin et al[16] demonstrated that there was indeed some fibrin in the subendothelium of the renal glomeruli and in the decidual segment of spiral arteries of pre-eclamptic patients. Hypofibrinolysis during pregnancy may be due to the effects of placenta-mediated inhibitors on fibrinolytic activity[17]. The evidence supporting this explanation is the increase in fibrinolysis after delivery.

Whether platelets of pre-eclamptic subjects were induced hyperacively by their over synthesis of TXA_2 further investigation is required. The finding should develop more effective management or prevention of this pathology. That is, if the result of the investigation show that more TXA_2 are synthesized in pre-eclamptic pregnancy, easy and safe management could be applied by administration of ASA or any cyclo-oxygenase inhibitors. If TXA_2 synthesis is not significantly changed other types of anti-platelet drugs should be applied to overcome hyperaggregated platelets.

Conclusion

Platelets of both NP, mild and severe PE were hypersensitive to collagen, adrenaline and ADP. After delivery only NP revealed significant decrease of their maximal aggregation. Fibrinolytic activity of PE, was under the normal range, after delivery it returned to normal.

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