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Changes of platelet parameters in early severe preeclampsia

Z.M. Wang*, Q.Y. Zhu*, J.F. Zhang, J.L. Wu, R. Yang, D.M. Wang

Department of Obstetrics, the First Affiliated Hospital of Xinjiang Medical University, Urumqi (China)

Summary

Objective: The aim of this study was to investigate the changes and clinical values of platelet parameters in different types of severe preeclampsia (SP). *Materials and Methods:* The pregnant women with SP or normal conditions were selected for the study, the platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW). and plateletcrit (PCT) were tested every four weeks, starting from 12^{+1} to 16 gestational weeks, to compare the difference in platelet parameters between SP and normal pregnant women. *Results:* PLT, MPV, and PDW of the early onset group exhibited statistically significant differences than the normal group from 20^{+1} gestational weeks, and PCT of the early onset group exhibited statistically significant differences than the normal group from 28^{+1} gestational weeks ($p < 0.05$); PLT, MPV, and PDW of the late onset group exhibited statistically significant differences than the normal group ($p < 0.05$), while PCT of the late onset group exhibited no statistically significant difference than the normal group from 12^{+1} gestational weeks until childbirth ($p > 0.05$). The comparison between the early onset group and the late onset group revealed that there existed statistically significant differences in PLT, MPV, and PDW ($p < 0.05$), but PCT showed no statistically significant difference throughout the pregnancy period ($p < 0.05$). *Conclusions:* The changes of platelet parameters in early onset SP patients were earlier than the late onset group, and the difference was statistically significant ($p < 0.05$). Measuring the platelet parameters could better reveal early-stage SP, thus guiding more personalized clinical treatments to better protect maternal and child safety.

Key words: Platelet parameters; Severe; Preeclampsia.

Introduction

Hypertension occurring in gestational period was collectively named as gestational hypertensive disorders, which exhibited hypertension and proteinuria as the clinical characteristic syndromes [1, 2]. Pregnancy could cause high blood pressure and could also aggravate the pre-existing hypertension [3]. The National High Blood Pressure Education Program Working Group (USA) proposed, in 2000, and had been recognized by the American Society of Obstetrics and Gynecology, that pregnancy-induced hypertension and pregestational hypertension were collectively recognized as gestational hypertensive disorders [4-6], which were divided into gestational hypertension, preeclampsia, eclampsia, chronic hypertension superimposed preeclampsia, and pregnancy plus chronic hypertension, based on the symptoms, signs, and clinical manifestations [7]. The occurrence of gestational hypertensive disorders was very common, and it was also one of common causes that led to an increase of maternal and perinatal morbidity and mortality. According to statistics, approximately 50,000 women worldwide die of eclampsia each year [8]. It was reported abroad that the incidence of gestational hypertensive disorders was 6.4% to 7.0% [9], while the average incidence rate in China was 9.4% [10] Studying the exact etiologies and pathogenesis of gestational hypertensive disorders have been an important research topic in the field of obstetrics and gynecology, in recent years, and the more generally accepted pathogenesis was the activation and damage theory of endothelial cells [11]. The vascular endothelium was a physiological interface, which separated blood cells, vascular wall collagen and smooth muscles, meanwhile, it might allow nutrients, metabolites, regulatory molecules, and phagocytes to penetrate the vascular basement membrane through complex metabolic and endocrine functions [12], thus preventing platelet aggregation and blood clotting, and regulating contractile response of vascular smooth muscles. Once the vascular endothelium is damaged, it might increase vascular permeability [13], glomerular protein leakage, tissue edema, blood concentration, procoagulant factors, and vasoconstriction factors [14], while reduce anti-clotting factors and vasodilators, resulting in platelet aggregation and thrombosis in the damaged parts [15]. With regards to the biochemical indicators [16], fibronectin, endothelin, thromboxane B2, nitric oxide, and anticoagulant were reduced [17]. Some scholars found the changes of blood clotting in preeclampsia [18], together with intravascular micro-coagulation, destruction of red blood cells, and thrombocytopenia, but there is no report assessing in which pregnancy stage these changes begin to change. As an important indicator of coagulation changes, platelet parameters including platelet counting (PLT), mean platelet volume (MPV), platelet distribution width

*Contributed equally.

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Table 1. — *PLT changes among the three groups (x10⁹/L, $\bar{x} \pm s$).*

Gestational week	Control group (n=200)		Early onset group (n=95)		Late onset group (n=105)	
	Cases	PLT	Cases	PLT	Cases	PLT
12^{+1}~16	147	204±47	63	209±41	90	201±37
16^{+1}~20	193	195±46	75	198±49	102	192±42
20^{+1}~24	177	201±52	84	191±47[a]	101	196±44
24^{+1}~28	189	195±35	89	171±38[ab]	104	195±56
28^{+1}~32	180	191±31	76	160±55[ab]	97	176±37[a]
32^{+1}~36	196	193±36	55	138±57[ab]	102	173±50[a]
36^{+1}~	199	188±51			74	167±55[a]

[a] Compared to the normal group; [b] compared to the late-onset group.

Table 2. — *MPV changes among the three groups (fl, $\bar{x} \pm s$).*

Gestational week	Control group (n=200)		Early onset group (n=95)		Late onset group (n=105)	
	Cases	MPV	Cases	MPV	Cases	MPV
12^{+1}~16	147	9.7±0.6	63	9.9±0.7	90	9.8±0.8
16^{+1}~20	193	9.8±0.7	75	10.0±0.7	102	9.9±0.7
20^{+1}~24	177	10.1±0.6	84	11.1±0.8	101	10.1±0.7
24^{+1}~28	189	0.9±0.7	89	11.5±0.7[ab]	104	10.6±0.9[a]
28^{+1}~32	180	10.1±0.5	76	12.9±0.9[ab]	97	10.8±0.9[a]
32^{+1}~36	196	10.1±0.7	55	14.3±2.9[ab]	102	11.3±1.0[a]
36+1~	199	10.2±0.8			74	11.8±1.8[a]

[a] Compared to the normal group; [b] compared to the late-onset group.

Table 3. — *PDW changes among the three groups (%, $\bar{x} \pm s$).*

Gestational week	Control group (n=200)		Early onset group (n=95)		Late onset group (n=105)	
	Cases	PDW	Cases	PDW	Cases	PDW
12^{+1}~16	147	10.91±1.54	63	10.85±1.55	90	10.78±1.41
16^{+1}~20	193	10.84±1.56	75	10.87±1.71	102	10.82±1.40
20^{+1}~24	177	10.85±1.38	84	11.97±1.82[a]	101	11.01±1.52
24^{+1}~28	189	10.82±1.42	89	12.32±2.26[ab]	104	11.75±1.78[a]
28^{+1}~32	180	11.02±1.67	76	14.90±2.73[ab]	97	12.22±1.82[a]
32^{+1}~36	196	10.95±1.61	55	17.12±3.05[ab]	102	13.16±1.96[a]
36^{+1}~	199	11.31±1.72			74	13.72±2.10[a]

[a] Compared to the normal group; [b] compared to the late-onset group.

Table 4. — *PCT changes among the three groups (%, $\bar{x} \pm s$).*

Gestational week	Control group (n=200)		Early onset group (n=95)		Late onset group (n=105)	
	Cases	PCT	Cases	PCT	Cases	PCT
12^{+1}~16	147	0.24±0.11	63	0.26±0,08	90	0.25±0.09
16^{+1}~20	193	0.23±0.08	75	0,23±0,06	102	0.22±0.09
20^{+1}~24	177	0.23±0.10	84	0.24±0.08	101	0.23±0.09
24^{+1}~28	189	0.21±0.07	89	0.22±0.07	104	0.22±0.05
28^{+1}~32	180	0.21±0.08	76	0.19±0.06[a]	97	0.20±0.07
32^{+1}~36	196	0.20±0.05	55	0.18±0.05[a]	102	0.19±0.08
36^{+1}~	199	0.20±0.05			74	0.19±0.05

[a] Compared to the normal group.

(PDW), and plateletcrit (PCT) have been included. The present study analyzed the changes of platelet parameters in different types of SP, then compared them with normal pregnant women, aiming to provide instructive meaning in clinic applications.

Materials and Methods

General Information

Two hundred SP patients, treated in the present hospital from January 2013 to June 2015, were selected and all met the diagnostic criteria proposed in the literature. According to the time of onset (set at 34 gestational weeks), and according to gestational ages, the patients were divided into the early onset group (n=95, gestational age < 34 weeks), aged 22 to 39 years, with a mean age of 27.5 ± 5.65 years, and the late onset group (n=105, gestational age ≥ 34 weeks), aged 22 to 37 years, with a mean age of 26.8 ± 6.17 years. Two hundred normal pregnant women, physically assessed in the same period, were selected as the control group, aged 20 to 37 years, with a mean age of 27.1 ± 6.21 years. Exclusion criteria [19]: with thrombotic or bleeding disorders, or diseases in blood system, liver and kidney, administrated aspirin and other drugs that might affect platelet functions, as well as pregnancy complications or severe internal or surgical complications. There was no statistically significant difference in age and gestation/delivery time among the three groups ($p > 0.05$) and hence were comparable. This study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Xinjiang Medical University. Written informed consent was obtained from all participants.

An automatic hematology analyzer was used to detect the blood routine indicators. Three ml periphery blood was sampled and placed into anticoagulant tube for the analysis. Main detection indicators included PLT, MPV, PDW, and PCT.

SPSS18.0 statistical software was used in the analysis. The measurement data are expressed as mean ± standard deviation ($\bar{x}$±s); the pairing information and the intergroup mean were compared with the *t*-test, the comparison of rate used the chi-square test, with $p < 0.05$ considered as statistically significant.

Results

PLT changes among the three groups

Compared to the control group, PLT in the early onset group exhibited statistically significant difference from 20^{+1} gestational weeks, and that in the late onset group exhibited statistically significant difference compared to the control group from 28^{+1} gestational weeks ($p < 0.05$). From 20^{+1} gestational weeks, PLT in the early onset group was statistically lower than in the late onset group ($p < 0.05$, Table 1).

MPV changes among the three groups

Compared to the control group, MPV in the early onset group exhibited statistically significant difference than the control group from 20^{+1} gestational weeks, and that in the late onset group exhibited statistically significant difference compared the control group from 24^{+1} gestational

weeks ($p < 0.05$). From 20^{+1} gestational weeks, MPV in the early onset group was statistically higher than the late onset group ($p < 0.05$, Table 2).

PDW changes among the three groups

Compared to the control group, PDW in the early onset group exhibited statistically significant difference from 20^{+1} gestational weeks, and that in the late onset group exhibited statistically significant difference than the control group from 24^{+1} gestational weeks ($p < 0.05$). From 24^{+1} gestational weeks, PDW in the early onset group was statistically lower than the late onset group ($p < 0.05$, Table 3).

PCT changes among the three groups

Compared to the control group, PCT in the early onset group exhibited statistically significant difference from 28^{+1} gestational weeks, while that in the late onset group exhibited no statistically significant difference compared to the control group and the early onset group during all gestational weeks ($p > 0.0$, Table 4).

Discussion

The current study suggested that systemic small artery spasm and endothelial injury were the main causes of preeclampsia [20, 21]. Once suffered from preeclampsia, the body's normal clotting, anticoagulation, and fibrinolysis, etc., would be destroyed, so that patient's blood would be in an abnormal hypercoagulable state, and there would be such situations as platelet aggregation and consumption [22, 13], which ultimately lead to higher blood pressure, edema, proteinuria, and other adverse consequences; organ perfusion would be then reduced, causing a serious threat to both mothers and babies. Because the platelet parameters in SP patients exhibit changes [23] than the normal population, detecting the changes of platelet parameters could better diagnose SP. The commonly used clinical parameters including PLT, MPV, PCT, and PDW, among which PLT reflects the production or aging situation of platelets, MPV is the mean volume of single platelet. Generally the MPV would be small during senescence, while large during growth or at mature stage; PDW represents the coefficient of variation of single platelet volume size and a smaller PDW suggests that body functions are more stable and normal. PCT represents the volume ratio of platelets in whole blood and is also an important parameter in measuring platelets.

In the normal population, although pregnancy had some effects on platelet parameters, such as MPV growth [24], etc., the impact ranges were less. Preeclampsia had more influences on platelet parameters. Some scholars indicated that SP patients exhibited significantly reduced platelets than in normal pregnant women, and after 20-28 gestational weeks, the relevant parameters had different degrees of difference than normal pregnant women [25].

The results of this study showed that PLT, MPV, and PDW of the early onset group exhibited statistically significant difference compared to the normal group from 20 gestational weeks, and PCT exhibited statistically significant difference compared to the normal group from 28 gestational weeks ($p < 0.05$), while the late-onset group exhibited statistically significant difference compared to the normal group in PLT, MPV, and PDW from 28, 24, and 25 gestational weeks, respectively. In this study, because of modern diagnostic tools, such as platelet parameters monitoring, the disease was discovered in time, and the termination of pregnancy was carried out on the basis of respecting patient's free will. As for the causes and mechanisms of SP-induced changes of platelet parameters, the existing literatures introduced the following [26]: the vascular endothelial cells are damaged, thus exposing the collagen fibers, so that the platelets aggregate and are consumed; the excessive activation of platelets is not required, therefore, hyperfunctioning is caused, and increases platelet consumption; microvascular spasm occurs and because of vascular endothelial hypoxia and ischemia, a large number of platelets are destroyed. According to the view points of existing research findings, the large number of platelet activation causing hyperfunctioning is the important cause in which SP could affect the changes of platelet parameters.

The results of this study showed that compared to the normal group, the platelet parameters in SP patients exhibited changes when they developed in a certain stage of pregnancy. In this study, in either the early or late onset group, MPV and PDW were higher compared to the normal group, while PLT was significantly lower compared to the normal group. As for PCT, only the early onset group exhibited statistically significant difference compared to the normal group from 28 gestational weeks ($p < 0.05$). MPV, PDW, and PLT had more clinical application values towards the early detection of SP.

This study showed that MPV, PDW, and PLT in the early-onset SP patients exhibited statistically significant difference compared to the normal group from 20 gestational weeks ($p < 0.05$), while MPV and PDW during the late onset, SP patients exhibited statistically significant difference compared to the normal group from 24 gestational weeks ($p < 0.05$). The time point when the early onset SP patients exhibited abnormal changes of platelet parameters was earlier than the late-onset SP patients, which was related to the relatively earlier onset, faster progression, and increased intensive activation, aggregation, hyperfunctioning, and consumption of platelets.

Given the negative impacts of SP on mothers and fetuses, it would exhibit great significance towards pregnant women and fetuses to undergo timely treatments. Currently, antiplatelet agent aspirin has been widely used

in clinical practice. This kind of drug can effectively destroy the activity of platelet cyclooxygenase, block the metabolism of arachidonic acid, damage the generation of TXA2, and thus effectively inhibit the aggregation and release of platelets, preventing thrombosis. Some scholars reported in pregnant women with such high risks of preeclampsia as chronic high blood pressure, history of kidney disease, with SP in previous pregnancy, the prophylactic application of aspirin could effectively reduce the incidence of preeclampsia, avoiding premature delivery, and better maintain the safety of pregnant women and perinatal children. Therefore, it was necessary to perform early diagnosis and targeted therapies towards the pregnant women with high risk of preeclampsia, thereby protecting the safety of mothers and fetuses.

The present study showed that SP was a great threat towards pregnant women and perinatal children, and the earlier the onset of SP, the greater the threat might be. In order to effectively maintain the safety of mothers and fetuses, it is necessary to strengthen the platelet monitoring during gestation period; through analyzing the changes of platelet parameters, preeclampsia can be detected earlier, so that targeted therapy could be performed. With regards to monitoring, it should be commenced from 20-24 gestational weeks, and some women at higher risk, it may be scheduled from 16 gestational weeks, enabling earlier detection of the disease and effective treatments.

In summary, monitoring the platelet parameters was simple and the results were reproducible and intuitive, thus exhibiting important clinical values in diagnosing SP. Monitoring the platelet parameters could guide the prediction, diagnosis, and treatment of disease, thus better serving pregnant women and perinatal children, while protecting their safety.

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Corresponding Author:
D.M. WANG,
Department of Obstetrics, The First Affiliated Hospital of Xinjiang Medical University
No. 137 Liyushan Nan Road, Urumqi 830054 (China)
e-mail: dongmeiwangcn@126.com