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Investigation of Mean Platelet Volume and Dipper/ Non-dipper Status in preeclamptic women during pregnancy and postnatal period

Preeklamptik Kadınlarda Gebelik ve Postnatal Periyotta Ortalama Platelet Volümü ve Dipper/Non-Dipper Durumunun Araştırılması

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ABSTRACT: ***Objective:*** Our aim was to determine mean platelet volume (MPV) changes between dipper and non-dipper preeclamptic women during pregnancy and postnatal period.
Material and Methods: We conducted the study of 17 preeclamptic women with dipper status and 12 with non-dipper status, versus 30 normotensive pregnant women. Fifty six women were studied again 6 months after birth to obtain reference data. 24-hour ambulatory blood pressure was measured by oscillometric device. Dipping profile is defined as a nocturnal blood pressure fall of 10 or more than 10% and non-dipping profile is defined as a nocturnal blood pressure fall of less than 10%. HGB, HCT, PLT and MPV levels were measured for all patients.
Results: Preeclamptic women with dipper and non-dipper status had a significantly higher MPV values than normotensive pregnant women did (10.4 ± 1.3, 10.1 ± 0.9 and 8.9 ± 1.9 fl, respectively; P=0.003). Furthermore, preeclamptic women with dipper and non-dipper status had a significantly higher MPV values than formerly preeclamptic women did (10.4 ± 1.3 vs. 8.5 ± 1.2, P=0.001 and 10.1 ± 0.9 vs. 8.5 ± 1.1 fl, respectively; P=0.002). But 6 months after birth, MPV values were not statistically different between all 3 groups (8.5 ± 1.1, 8.5 ± 1.1 and 8.9 ± 1.9 fl, respectively; P=0.588). In addition, MPV values were not different between dipper and non-dipper groups.
Conclusion: Preeclampsia pathogenesis may help to explain higher MPV values in preeclamptic women. However, since there is no difference between dipper subgroups, no additional information is available by MPV evaluation.
Key Words: Mean platelet volume (MPV); dipper; non-dipper; preeclampsia

ÖZET: ***Amaç:*** Amacımız dipper ve non-dipper preeklamptik kadınlar arasında, gebelikte ve postnatal periyotta ortalama platelet volümü (MPV) değişikliklerini saptamaktı.
Gereç ve Yöntem: Dipper durumuna sahip 17 preeklamptik kadın ve non-dipper durumuna sahip 12 preeklamptik kadına karşılık 30 normotansif gebe kadınla çalışmayı gerçekleştirdik. Referans bilgisi sağlamak için doğumdan 6 ay sonra 56 kadın ile tekrar çalışıldı. Osilometrik cihazla 24 saat ambulatuar kan basıncı ölçüldü. Dipping profili, noktürnal kan basıncında %10 veya daha fazla düşme olarak tanımlandı ve non-dipping profili, noktürnal kan basıncında %10'dan daha az düşme olarak tanımlandı. Tüm hastalar için HGB, HCT, PLT ve MPV düzeyleri ölçüldü.
Bulgular: Dipper ve non-dipper durumuna sahip preeklamptik kadınlar, normotansif gebe kadınlara göre belirgin derecede yüksek MPV değerlerine sahipti (10.4 ± 1.3, 10.1 ± 0.9 ve 8.9 ± 1.9 fl, sırasıyla; P=0.003). Dahası, dipper ve non-dipper durumuna sahip preeklamptik kadınlar, önceden preeklamptik olan kadınlara göre belirgin derecede yüksek MPV değerlerine sahipti (10.4 ± 1.3 vs. 8.5 ± 1.2, P=0.001 ve 10.1 ± 0.9 vs. 8.5 ± 1.1 fl, sırasıyla; P=0.002). Ancak, doğumdan 6 ay sonra, MPV değerleri, 3 grup arasında istatistiksel olarak farklı değildi (8.5 ± 1.1, 8.5 ± 1.1 ve 8.9 ± 1.9 fl, sırasıyla; P=0.588). Ayrıca, MPV değerleri dipper ve non-dipper grupları arasında farklı değildi.
Sonuç: Preeklampsi patogenezi preeklamptik kadınlarda yüksek MPV değerlerini açıklamada yardımcı olabilir. Bununla beraber dipper alt grupları arasında farklılık olmadığı için MPV değerlendirmesi yoluyla ek bilgi mümkün değildir.
Anahtar Sözcükler: Ortalama platelet volümü (MPV); dipper; non-dipper; preeklampsi

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INTRODUCTION

Preeclampsia is a common disease of human pregnancy and a leading cause of both, maternal and

neonatal morbidity and mortality, respectively (1). It affects approximately 5% of all pregnant women (2). The etiology of preeclampsia is unknown but major pathophysiologic mechanism has focused on the failure of the normal invasion of trophoblast cells by the placenta (3). Additionally, there has also been interest in the role of platelets in the pathophysiology of preeclampsia. As was shown in many studies that increased platelet activation triggered by endothelial injury may cause platelet consumption and thus, the joining of new and big volumed platelets to circulation in preeclampsia (4-6).

Blood pressure measurement plays a central role in the screening and management of hypertension during pregnancy. Ambulatory blood pressure monitoring (ABPM) can be used in hypertension in pregnancy and is helpful for screening and management (7,8). With ABPM, the information is obtainable about blood pressure (BP) during the night and dipper and non-dipper BP status are determined. Dipping profile is defined as a nocturnal blood pressure fall of 10 or more than 10% and non-dipping profile is defined as a nocturnal blood pressure fall of less than 10%. These measures may reflect the prognosis of preeclampsia although it is a new onset hypertensive event. Because of the fact that hypertensive patients with a non-dipping BP pattern compared with dippers have more target organ damage (9) and maternal blood pressure is related to elevated platelet volumes (4) we aimed to determine mean platelet volume (MPV) changes among currently and formerly dipper and non-dipper preeclamptic patients.

MATERIAL AND METHODS

We studied 59 pregnant women consecutively during the third trimester of pregnancy. The study group included 30 normotensive pregnant women, 17 dipper preeclamptic women and 12 non-dipper preeclamptic women. Fifty six women were studied again 6 months after delivery to obtain reference data. This group included 27 formerly normotensive pregnant women (file records of 3 in normotensive pregnant women were not reached 6 months after delivery), 17 formerly dipper preeclamptic women and 12 formerly non-dipper preeclamptic women. The study was carried out at Afyonkarahisar Kocatepe University Department of Obstetrics and Gynecology by scanning the file records retrospectively.

Preeclampsia was defined as a systolic blood pressure (SBP) of ≥140 mmHg or diastolic blood pressure (DBP) of ≥90 mmHg occurring after 20 weeks of gestation in a woman with previously normal blood pressure, and proteinuria ≥0.3 g/24 h (3). Exclusion criteria for preeclamptic and normotensive pregnant women were diabetes mellitus, thyroid diseases, multiple pregnancies, cardiovascular diseases, smoking, or renal diseases. All 30 normotensive pregnant women had blood pressure <140/90 mmHg. The following laboratory tests were done for all women on admission: hemoglobin (HGB), hematocrit (HCT), platelet count (PLT), MPV, urinalysis, uric acid, blood urea nitrogen, creatinine, transaminases and serum electrolytes. In preeclamptic women, 24-hour urinary protein was measured, also.

On admission, SBP and DBP measurements were performed by calibrated standard mercury sphygmomanometer after 15 min of rest in a 30o left lateral position so as to prevent gravid uterus pressure. Pulse pressure (PP) was calculated as the difference between SBP and DBP. Mean arterial pressure (MAP) was calculated as DBP plus 1/3 of PP.

The SBP, DBP, and heart rate (HR) of each participant were automatically measured every 20 minutes from 6 AM to 10 PM, and every 30 minutes during the night for 24 consecutive hours with a properly calibrated SpaceLabs 90217 oscillometric device (Spacelabs Inc., Redmond Washington); the ABPM device was recalibrated approximately every six months. The nurse placed an appropriately sized blood pressure cuff on the subject's non-dominant arm, and removed it 24 h later. The ABPM device was carried for one 24 h period on admission during the third trimester of pregnancy. The data were considered adequate when a minimum of 70 valid recordings were obtained in 24 h, with at least two recordings per hour during the nighttime. ABPM always started between 10 AM and 1 PM. Blood pressure measurements that occurred after 6 AM and before 10 PM were regarded as "daytime" measurements, while measurements that occurred between 10 PM and 6 AM were designated as "nighttime" measurements. Average 24 h, daytime and nighttime SBP and DBP, 24 h, daytime and nighttime PP were evaluated (10).

For all women, 20 ml of blood was obtained by antecubital venepuncture without stasis and we measured MPV in a blood sample collected in citrate (v : v, 4 : 1). It is well known that MPV changes during storage of blood samples, so the time

between sampling and tube reading was approximately 10 minutes. A Sysmex XT- 2000i (Sysmex Ltd, Buckinghamshire, UK) was used for whole blood counts.

Statistical analysis

All parametric results were expressed as mean ± standard deviation for each group. The results were evaluated statistically using One-way analysis of variance (ANOVA) (Table 1,2) and paired samples t-test (Table3). Multiple comparisons (Table 1) were evaluated with Tukey test those were homogeneous variances and Tamhane test those were not homogeneous variances. P value less than 0.05 was considered to be statistically significant.

***Table 1**. Demographic data and laboratory parameters of the study group.*

	Normotensive pregnant (1)	Dipper preeclamptic (2)	Non-dipper preeclamptic (3)	P
Age (years)	25.1 ± 4.0	28.5 ± 4.9	26.7 ± 6.2	NS
Parity	0.9 ± 0.9	1.1 ± 1.4	1.3 ± 2.4	NS
Gestational age on admission (weeks)	35.2 ± 2.8	34.1 ± 3.0	33.4 ± 3.2	NS
Systolic BP on admission (mmHg)	111 ± 9	157 ± 12[a,b]	151 ± 9[c]	<0.001
Diastolic BP on admission (mmHg)	67 ± 8	102 ± 7[a,b]	99 ± 6[c]	<0.001
Mean arterial pressure (mmHg)	82 ± 8	125 ± 19[a,b]	116 ± 6[c]	<0.001
Pulse pressure (mmHg)	43 ± 7	55 ± 9[a,b]	52 ± 7[c]	<0.001
HGB (g/dL)	12.4 ± 1.2	12.0 ± 1.9	11.6 ± 1.6	NS
PLT (10^6 /mm^3)	237 ± 97	225 ± 79	214 ± 79	NS
HCT (%)	36.9 ± 3.1	36.9 ± 4.7	36.2 ± 5.1	NS
MPV (fl)	8.9 ± 1.9	10.4 ± 1.3[a,b]	10.1 ± 0.9[c]	0.003
Creatinine (mmol/L)	0.5 ± 0.1	0.6 ± 0.1[a,b]	0.7 ± 0.1[c]	0.001

Systolic BP on admission, [a] p<0.001 vs. 1; [b] p=0.234 vs. 3; [c] p<0.001 vs. 1
Diastolic BP on admission, [a] p<0.001 vs. 1; [b] p=0.352 vs. 3; [c] p<0.001 vs. 1
Mean arterial pressure, [a] p<0.001 vs. 1; [b] p=0.217 vs. 3; [c] p<0.001 vs. 1
Pulse pressure, [a] p<0.001 vs. 1; [b] p=0.662 vs. 3; [c] p=0.001 vs. 1
MPV, [a] p=0.005 vs. 1; [b] p=0.872 vs. 3; [c] p=0.012 vs. 1
Creatinine, [a] p=0.026 vs. 1; [b] p=0.541 vs. 3; [c] p=0.002 vs. 1
NS: not significant, BP: blood pressure
Dipper means a nocturnal BP fall of 10 or more than 10%
Non-dipper means a nocturnal BP fall of less than 10%.

***Table 2**. Hematologic parameters of formerly preeclamptic and normotensive pregnant women.*

	Formerly normotensive pregnant	Formerly dipper preeclamptic	Formerly non-dipper preeclamptic	P
HGB(g/dL)	12.7 ± 1.1	12.6 ± 0.6	12.5 ± 1.0	NS
PLT(10^6/mm^3)	228 ± 96	225 ± 2	224 ± 52	NS
HCT (%)	37.1 ± 2.9	37.1 ± 1.7	36.9 ± 1.4	NS
MPV (fl)	8.9 ± 1.9	8.5 ± 1.1	8.5 ± 1.1	NS

NS: not significant
Dipper means a nocturnal BP fall of 10 or more than 10%
Non-dipper means a nocturnal BP fall of less than 10%.

***Table 3**. Hematologic parameter changes in currently and formerly preeclamptic women.*

	Dipper preeclamptic	Formerly dipper preeclamptic	P	Non-dipper preeclamptic	Formerly non-dipper preeclamptic	P
HGB(g/dL)	11.9 ± 1.5	12.6 ± 0.6	NS	11.5 ± 1.7	12.5 ± 0.6	0.005
PLT($10^6$$mm^3$)	225 ± 79	225 ± 2	NS	208 ± 79	224 ± 51	NS
HCT (%)	37.0 ± 4.8	37.1 ± 1.7	NS	36.0 ± 5.2	37.0 ± 1.4	NS
MPV (fl)	10.4 ± 1.3	8.5 ± 1.2	0.001	10.1 ± 0.9	8.5 ± 1.1	0.002

NS: not significant
Dipper means a nocturnal BP fall of 10 or more than 10%
Non-dipper means a nocturnal BP fall of less than 10%.

RESULTS

Demographic data and laboratory parameters of the study group are shown in Table 1. The groups were similar with regard to age, parity, gestational age on admission and hematologic parameters like HGB, PLT and HCT as shown in Table 1. As expected, preeclamptic women had significantly higher SBP, DBP, MAP and PP considering normotensive pregnant women. Preeclamptic women with dipper and non-dipper status had a significantly higher MPV values than did normotensive pregnant women (10.4 ± 1.3, 10.1 ± 0.9 and 8.9 ± 1.9 fl, respectively; P=0.003).

Hematologic parameters of all 3 groups 6 months after birth were given in Table 2. Hematologic parameter changes in preeclamptic women during pregnancy and postnatal period were given in Table 3. Preeclamptic women with dipper and non-dipper status had a significantly higher MPV values than did formerly ones (10.4 ± 1.3 vs. 8.5 ± 1.2, P=0.001 and 10.1 ± 0.9 vs. 8.5 ± 1.1 fl, respectively; P=0.002). But 6 months after birth MPV values were not statistically different between all 3 groups (8.5 ± 1.1, 8.5 ± 1.1 and 8.9 ± 1.9 fl, respectively; P=0.588). In addition, MPV values were not different neither during pregnancy (10.4 ± 1.3 vs. 10.1 ± 0.9 fl, P=0.872) nor postnatal period (8.5± 1.1 vs. 8.5± 1.1 fl, P=0.999) between dipper and non-dipper groups.

DİSCUSSİON

Increased platelet activation is known in normal pregnancy but this is more evident in hypertensive states of pregnancy (11,12). Incomplete invasion to spiral arteries by the trophoblasts causes an increase in the release of vasoactive amines, contributing to systemic endothelial dysfunction and it constitutes major pathophysiology in preeclampsia (13,14) besides, there are increasing number of proves has been emerged about pathogenesis of preeclampsia, recently. Occurance of endothelial damage can cause increased activation of platelets which has an important role of appearing thrombus on the region and because of increased platelet activation, increased platelet consumption and thus, increased joining of new and big volumed, more reactive platelets occurs (4-6, 15-17). Our results suggest that preeclamptic women has higher MPV according to normotensive pregnant women. Moreover, in our study we showed that formerly dipper and non-dipper preeclamptic women had no significant MPV measurements difference with formerly normotensive pregnant women. It may be originated from increased platelet activation and thus increased MPV caused by systemic endothelial dysfunction in preeclampsia rapidly return to normalcy after birth. Similarly, Järemo et. al demonstrated that MPV measurements were decreased 3 to 12 months after birth (4).

Several laboratory techniques have been developed to detect platelet activation. These were platelet volumes and sizes, radiolabeling methods, aggregometry procedures, adhesion molecules etc.(18). It was shown that platelet size determine platelet function independently (19). But MPV measurements have a few important limitations. Chosen method for measurement (20), chosen anticoagulant for collection and the time until considering MPV measurement (21,22) may influence the power of MPV measurement. In that case, adhesion molecules that used to show platelet activation seem more sensitive (4,23). In this study, for indicator of platelet activation we used MPV instead of other markers and this may be limitation of our study.

Maternal blood pressure follow-up give a very important data relating with maternal and fetal well-being in preeclampsia. Casual BP measurements have traditionally constituted the principal modality for the assessment and management of hypertension, however, traditional blood pressure monitoring has limitations (24), in that case, 24-hour ABPM although there are no randomised controlled trials can be used in hypertension in pregnancy and is helpful for screening and management (7,8). Through 24-hour monitoring the information is obtainable about BP during the night and dipper and non-dipper BP status can be determined. Hypertensive patients with a non-dipping BP pattern compared with dippers have more target organ damage (9,25) but it should be noted that dipper and non-dipper BP measurements have several shortcomings. For instance, daytime inactivity, poor sleep quality and nighttime activity may change the BP measurements and may affect the estimating power of ABPM (26,27). In addition, repeated daytime and nighttime measurements may give different results (28). In our study, although preeclamptic patients had higher MPV compared with normotensive ones, there were no statistically difference between dipper and non-dipper preeclamptic patients about MPV. This may be related with MPV measurement methods, dipper and non-dipper status measurement method or only a small numbers of study group.

In conclusion, preeclampsia pathogenesis may help to explain higher MPV values in preeclamptic women. However, since there is no difference between dipper and non-dipper groups neither in pregnancy nor in postnatal period, no additional information is available by MPV evaluation.

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