



Relationship Between Retinopathy and Mean Platelet Volume

Retinopati Şiddeti ile Ortalama Trombosit Hacmi Arasındaki İlişki

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Abstract

Objective: Platelet activation is thought to play a role in the angiogenesis process involved in the pathophysiology of retinopathy of prematurity (ROP). We planned this study to investigate whether the mean platelet volume (MPV), used to assess platelet activation, could be used as a biomarker in the diagnosis and treatment of ROP.

Material and Method: In our study, we evaluated infants who underwent ROP examination among infants born at 32 weeks or less and/or 1500 grams or less as well as infants who had more than these values but experienced a bad neonatal period. These patients were divided into two groups as those with and without ROP, and in those with ROP group, as requiring treatment and not requiring treatment. We recorded the patients' identity, maternal characteristics, antenatal/natal/postnatal features, and complications during follow-up, ROP control times, and complete blood count parameters (platelet count, MPV, platelet count/MPV). Primarily, we evaluated the differences of platelet parameters, especially the MPV values, between treatment requiring ROP and non-treatment requiring ROP groups and secondarily, we evaluated the correlation between scanned parameters and ROP development.

Results: Of the 144 patients included in the study, 49 patients (34%) had ROP and 25 patients (16.6%) had ROP requiring treatment. There were statistically significant differences between patients who were diagnosed with ROP and who were not, in terms of gestational age, birth weight, respiratory distress syndrome, surfactant use, duration of oxygen use, intraventricular hemorrhage, patent ductus arteriosus, neonatal sepsis, number of blood transfusions, necrotizing enterocolitis, bronchopulmonary dysplasia and time to catch up birth weight. However, there was no significant difference in terms of MPV, platelet count and platelet/MPV ratio. The gestational week, invasive ventilation day and duration of oxygen use, BPD and time to catch up birth weight were found to be statistically high in treatment-requiring rather than non-treatment-requiring ROP groups. There was no significant difference in MPV, platelet count, platelet/MPV ratio among these groups. A statistically significant difference was found in the most advanced stage ROP and plus existence in the treatment requiring ROP group.

Conclusion: As a result of our study, we could not find enough data to say that MPV is a marker that can be used in the diagnosis of ROP and in measuring the severity of retinopathy. We suggest that more studies should be done on this subject.

Keywords: Prematurity, retinopathy of prematurity, mean platelet volume

Öz

Amaç: Prematüre retinopatisi (Retinopathy of prematurity-ROP) patofizyolojisinde yer alan angiogenezis sürecinde platelet aktivasyonunun rolü olduğu düşünülmektedir. Platelet aktivasyonunu değerlendirmek için kullanılan ortalama platelet hacmi (Mean platelet volüm-MPV)'nin ROP tanı ve tedavisinde de kullanılabilir bir belirteç olup olmayacağını araştırmak amacıyla bu çalışmayı planladık.

Gereç ve Yöntem: Biz çalışmamızda 32 hafta ve altında ve/veya 1500 gram ve altında doğan bebeklerin yanı sıra hafta ve ağırlığı bu değerlerden fazla olup kötü bir yenidoğan süreci geçiren bebeklerden, ROP muayenesi yapılan hastaları değerlendirmeye aldık. Bu hastaları ROP gelişen ve gelişmeyen; ROP gelişen hastaları da tedavi gerektiren ve gerektirmeyen şeklinde iki gruba ayırdık. Hastaların kimlik bilgileri, maternal özellikleri, antenatal/natal/postnatal özellikleri, takipleri sırasında gelişen komplikasyonlar, ROP kontrol zamanları ve doğdukları gün bakılan tam kan parametrelerini (platelet sayısı, MPV, platelet sayısı/MPV) kaydettik. Primer olarak ROP tedavisi gerektiren ve gerektirmeyen hastaların trombosit parametreleri, özellikle MPV değerleri arasındaki farklılığı sekonder olarak taranmış olan parametreler ile ROP gelişimi arasındaki korelasyonu değerlendirdik.

Bulgular: Çalışmaya dahil edilen 144 hastadan 49 (%34)'unda ROP, 25 (%16.6)'ın de tedavi gerektiren ROP saptandı. ROP tespit edilen hastaların gebelik yaşı, doğum ağırlığı, RDS görülme sıklığı, sürfaktan kullanımı, oksijen kullanım süresi, intraventriküler kanama, PDA, neonatal sepsis, eritrosit transfüzyon sayısı, NEK, BPD ve doğum ağırlığını yakalama zamanı ROP tespit edilmeyenlere oranla yüksek tespit edildi. Ancak MPV, platelet sayısı ve platelet/MPV oranı açısından anlamlı fark bulunmadı. Tedavi gerektiren ve gerektirmeyen ROP grupları arasında ise gebelik yaşı, invaziv ventilasyon günü ve toplam oksijen kullanım süresi, BPD ve doğum ağırlığını yakalama zamanı tedavi gerektirmeyen gruba oranla yüksek bulundu ve bu sonuçlar istatistiksel olarak anlamlıydı. Bu gruplar arasında MPV, platelet sayısı, platelet/MPV oranı açısından anlamlı fark bulunmadı. Tedavi gerektiren ROP grubunda en ileri evre ve plus varlığı açısından istatistiksel olarak anlamlı yükseklik tespit edildi.

Sonuç: Çalışmamızın sonucunda MPV'nin ROP tanısında ve retinopati şiddetini ölçmede kullanılabilir bir belirteç olduğunu söylemek için yeterli veri bulamadık ve bu konu ile ilgili daha fazla çalışmalar yapılması gerektiğini önermekteyiz.

Anahtar Kelimeler: Prematürite, premature retinopatisi, ortalama trombosit hacmi



INTRODUCTION

Retinopathy of prematurity (ROP), first reported by Terry in 1942, is a physiopathological condition that occurs due to abnormal proliferation of retinal vessels in preterm babies but its pathogenesis is not fully known.^[1] Despite the increased possibilities of effective screening and early treatment, the fact that babies born earlier and with lower birth weight become viable causes an increase in the frequency of severe ROP cases located in the posterior pole.^[2]

Although many etiological factors have been considered in the development of ROP, the most well-known risk factors are low birth weight and gestational week.^[3]

Recent studies have shown that platelets play a role in the etiology of vascular diseases in the process of angiogenesis. It is known that there are changes in thrombocyte functions especially in obstructive vascular diseases. Therefore, it suggests that platelet activation may have a possible role in the pathogenesis of ROP.^[4]

Mean platelet volume (MPV) is an important marker that can be used in the evaluation of platelet activity. It is known that large platelets are more metabolically and enzymatically active than small ones. For this reason, we planned this study to show the possible relationship between ROP requiring treatment and MPV and whether MPV can be used as a marker in the diagnosis and treatment of ROP.^[5]

MATERIAL AND METHOD

This thesis study was initiated after receiving the Ethics Committee Approval with the decision of the Ethics Committee of Medicine and Non-Medical Device Researches Ethics Committee of Necmettin Erbakan University Meram Faculty of Medicine, dated 04/14/2017 and numbered 2017/866.

For the study, 144 cases that were followed up and evaluated for ROP in Necmettin Erbakan University Meram Medical Faculty Neonatal Intensive Care Unit between January 2016 and May 2017 were retrospectively analyzed. These patients were compared in terms of their demographic characteristics (**Table 1**), as well as platelet count, MPV, and platelet/MPV ratios in complete blood counts were taken when they were diagnosed with ROP. The cases in requiring and not requiring treatment groups were compared in terms of platelet count, MPV, platelet/MPV ratios as well as the highest stage, highest zone, presence of plus and first ROP detection time.

In this study, SAS University Edition 9.4 program was used for statistical analysis. In the analysis of parameters conforming to normal distribution, Independent sample t test was used to compare two groups and the results were reported as mean and standard deviation. Continuous variables not conforming to normal distribution were evaluated with the Mann-Whitney U test and the results were reported as median (Q1-Q3). Chi-square and Fisher tests were used to examine the relationship between categorical variables. The results were evaluated at the significance level of $p < 0.05$.

Table 1. Patient's demographic characteristics

	ROP diagnosed group (n=49)	non-ROP group (n=95)	p value
Maternal age (mean±SD)	29.12±6.25	28.51±5.67	0.55
Gestational age (weeks) (mean±SD)	28±2	31±2	<0.0001
Gender (n) (%)			
Girl	24 (49%)	48 (50.5%)	0.86
Boy	25 (51%)	47 (49.5%)	
Birth weight (grams) (mean±SD)	1055.3±292.1	1436.9±322.1	<0.0001
Birth way (n) (%)			
NSVY	9 (18.4%)	7 (7.4%)	0.055
C/S	40 (81.6%)	88 (92.6%)	
Grouping by birth weight (n) (%)			
SGA	5 (10.2%)	14 (14.7%)	0.43
AGA	44 (89.8%)	79 (83.2%)	
LGA	0 (0%)	2 (2.1%)	
Multiple pregnancies (n) (%)			
Single	38 (77.6%)	75 (78.9%)	0.88
Twin	10 (20.4%)	17 (17.9%)	
Triplets	1 (2%)	3 (3.2%)	
In vitro fertilization (n) (%)			
Yes	6 (12.2%)	13 (13.7%)	0.81
No	43 (87.8%)	82 (86.3%)	
Maternal steroid use (n) (%)			
No	13 (26.5%)	24 (25.3%)	0.32
Single dose	17 (34.7%)	23 (24.2%)	
Two doses	19 (38.8%)	48 (50.5%)	
Chorioamnionitis (n) (%)			
Yes	8 (16.3%)	12 (12.6%)	0.54
No	41 (83.8%)	83 (87.4%)	
Preeclampsia/Eclampsia (n) (%)			
Yes	13 (26.5%)	38 (40%)	0.14
No	36 (73.5%)	57 (60%)	
Maternal Diabetes (n) (%)			
Yes	3 (6.1%)	7 (7.4%)	0.78
No	46 (93.9%)	88 (92.6%)	

RESULTS

As a result of the evaluation of the patients, ROP was detected in 49 patients and ROP was not detected in 95 patients. 49 patients with ROP were divided into two groups as requiring and not requiring treatment. While the number of patients requiring treatment was 24, the number of patient's not requiring treatment was 25.

When MPV, platelet counts and platelet/MPV ratios of the groups with and without ROP were examined, no statistically significant difference was found between the groups for all three parameters (**Table 2**). Mean MPV values were 9.81 ± 1.76 f/L in the group with ROP, and 9.55 ± 1.57 f/L in the group without ROP ($p=0.38$). Mean platelet values were 220.9 ± 118.7 $10^3/\mu\text{L}$ in the group with ROP and 229.1 ± 80.9 $10^3/\mu\text{L}$ in the group without ROP ($p=0.63$). Mean Platelet/MPV ratios were 23.2 ± 13.6 in the group with ROP, and 24.7 ± 9.8 in the group without ROP ($p=0.46$). Mean Platelet/MPV ratios were 23.2 ± 13.6 in the group with ROP, and 24.7 ± 9.8 in the group without ROP ($p=0.46$).

Table 2: MPV, platelet values and platelet/MPV ratios of the groups with and without ROP

	ROP detected group (n=49)	ROP not detected group (n=95)	p value
MPV (f/L) (mean±SD)	9.81±1.76	9.55±1.57	0.38
Platelet (10 ³ /μL) (mean±SD)	220.9±118.7	229.1±80.9	0.63
Platelet/MPV ratio (mean±SD)	23.2±13.6	24.7±9.8	0.46

When the patients in the group with ROP were divided into subgroups requiring treatment and not requiring treatment, and when MPV, platelet numbers and platelet/MPV ratios of the groups were examined, no statistically significant difference was found between the groups for all three parameters (**Table 3**). Mean MPV values were 9.54±1.73 f/L in the ROP requiring treatment group and 10.06±1.79 f/L in the ROP not requiring treatment group (p=0.301). Mean platelet values were 208.6±117.8 10³/μL in the ROP requiring treatment group and 232.8±120.7 10³/μL in ROP not requiring treatment group (p=0.48). The platelet/MPV ratios were 22.78±14.9 in the ROP requiring treatment group and 23.74±12.5 in the ROP not requiring treatment group (p=0.81).

Table 3: MPV, platelet values and platelet/MPV ratios of the groups requiring and not requiring treatment.

	ROP group requiring treatment (n=24)	ROP group not requiring treatment (n=25)	p value
MPV (f/L) (mean±SD)	9.54±1.73	10.06±1.79	0.301
Platelet (10 ³ /μL) (mean±SD)	208.6±117.8	232.8±120.7	0.48
Platelet/MPV ratio (mean±SD)	22.78±14.9	23.74±12.5	0.81

Table 4. Evaluation of statistically significant clinical findings of ROP groups requiring and not requiring treatment.

	Treatment requiring ROP group (n=24)	Treatment not requiring ROP group (n=25)	p value
Invasive ventilation time (days) (median)	17 (4-30)	2 (0-7)	0.018
Total oxygen use (days) (median)	58.5 (38-83)	30 (13-56)	0.01
BPD (n) (%)			
Yes	16(66.7%)	8(32%)	0.015
No	8(33.3%)	17(68%)	
Day to catch up birth weight (day) (mean±SD)	15.45±6.93	11.8±4.33	0.031

DISCUSSION

Parallel to the developments in neonatal care in our country, the increase in the survival chances of premature babies with a much smaller gestational age (GA) and birth weight (BW) causes ROP, which can cause vision problems and blindness, to be a more frequent problem. In a multi-center study conducted by the Turkish Neonatal Society in 2014, the incidence of ROP in preterm babies with very low birth weight was found to be 42%, and the incidence of advanced stage ROP was 8.2%.^[5] In our study, we found the incidence of ROP as 34% and ROP requiring treatment as 16.6% in our premature babies.

ROP is an abnormal vascularization process triggered by prematurity and its associated negative processes.^[6] In our study, we aimed to show the effect of platelet function parameters, which is one of these factors, on the development of ROP.

Platelets have been shown to play a role in the etiology of vascular diseases. Various studies have reported that MPV values are higher, especially in occlusive vascular diseases, compared to the normal population.^[7,8]

The relationship between MPV and many diseases has been examined in the literature. Platelets with a large MPV value are more reactive than platelets with a small MPV, produce more thromboxane A2, express more glycoprotein Ib and glycoprotein IIb/IIIa. They aggregate more easily.^[9]

The relationship between MPV and ROP has also been recently considered. In the study of Çekmez et al, MPV was measured in the cord blood of 272 patients with a gestational week of <34 and a birth weight of <1500 g, and this parameter was repeated in the first three days of their lives and there was no significant difference in MPV values in both groups with and without ROP.^[10] In another study, laser-treated ROP patients constituted the case group, while those who did not develop ROP and those with stage 1 ROP were included in the control group, and the most recent platelet and MPV values of the patients were recorded.^[11] MPV values in the ROP requiring laser treatment group were statistically significantly higher than in the control group, but no significant difference was found in terms of platelet and MPV/platelet ratio. In addition, it was seen that as the MPV value increased, there was a 1.94 fold increase in ROP risk. It was concluded that MPV, used as the most common measure of platelet size, is a potential marker of platelet reactivity. In our study, we evaluated MPV, platelet counts and platelet/MPV ratios in complete blood count on the first day of life in groups with and without ROP, but we could not find a statistically significant difference between the groups. We also compared these parameters between the ROP requiring treatment and ROP not requiring treatment groups and likewise, we could not find a statistically significant difference between these groups. Although we attribute the inadequacy of our study to show the relationship between MPV and retinopathy to the low number of our patients, we believe that evaluating these parameters together with the results not only in the blood tests taken on the first day of life but also in the intermittent blood counts will help us more in understanding the relation of MPV with the presence and severity of retinopathy.

There are studies in the literature investigating the parameters associated with retinopathy between ROP requiring treatment and ROP not requiring treatment groups.^[12] In our study, we found that gestational week, invasive ventilation and total oxygen use time, BPD and day to catch up birth weight were higher in the ROP requiring treatment group compared to the group that did not require treatment, and these results were statistically significant. We compared the most advanced stage, the most advanced zone, the presence of plus and the first age (in days) which was ROP detected parameters

between the groups, and we found a statistically significant increase in the most advanced stage and presence of the plus in the ROP requiring treatment group. These results obtained in our study supported that the presence of stage and plus are important parameters in the treatment decision.

CONCLUSION

In conclusion, there are limited studies in the literature investigating the relationship between MPV and ROP. As a result of our study, we cannot say that MPV is a marker that can be used in the diagnosis of ROP and in measuring its severity. We think more numerous and more comprehensive studies are needed to understand the relationship between MPV, which is used to show the activity of platelets, which is known to have a role in the etiology of vascular diseases, and the presence or severity of retinopathy. In addition, we think that screening premature babies in neonatal units for retinopathy and early referral of risky babies to a limited number of treatment centers will be of great importance in preventing blindness due to prematurity.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval was obtained from the Ethics Committee of Medicine and Non-Medical Device Researches Ethics Committee of Necmettin Erbakan University Meram Faculty of Medicine, dated 04/14/2017 and numbered 2017/866.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

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