Original Article

Iran J Ped Hematol Oncol. 2018, Vol 8.No 4, 221-227

The Evaluation of Mean Platelet Volume in Neonates with Intraventricular Hemorrhage and Sepsis

Mahbod Kaveh MD[1], Kamyar Kamrani MD[1,*], Shiva Akhbari MD[1]

1. Tehran university of medical Sciences, Tehra, Iran
*Corresponding author: Kamyar Kamrani, MD, Tehran university of medical Sciences, Tehra, Iran. E-mail: kamyarkamrani48@gmail.com

Received: 01 September 2017 **Accepted:** 18 June 2018

Abstract

Background: Neonatal sepsis is a generalized bacterial infection which occurs in the first month of life. Intraventricular hemorrhage is the most common intracerebral disorder which occurs in premature neonates. Mean Platelet Volume (MPV) is considered as a marker of intraventricular hemorrhage (IVH) in some studies. The aim of this study was to evaluate the impact of MPV on IVH and sepsis in neonates.

Materials and methods: In this retrospective case-control study, 20 premature neonates with sepsis and 20 with sepsis and intraventricular hemorrhage were considered as case groups and 20 premature neonates without sepsis and IVH were regarded as control group. Demographic data as well as patients' data on IVH presence, IVH grading, mortality, platelet account, and MPVon the first and third days after birth were recorded using their medical files. After data collection, analysis was performed using SPSS (version 21) and running descriptive and analytical methods (T test, ANOVA and Chi square test).

Results: In this study, 10 newborns (50%) in the sepsis group, 13 newborns (65%) in the IVH – sepsis group, and 10 newborns (50%) in the control group were male (P = 0.523). Mean ± standard deviation of gestational age and weight at birth were significantly lower in the IVH and sepsis group in comparison with the other two groups (P-value < 0.001). Considering platelet count on first day, no significant difference was observed among three groups; however, it was lower in the control group than the sepsis group as well as the IVH and sepsis group (P=0.004). Gender, birth weight, gestational age, onset of sepsis, and presence of respiratory distress syndrome (RDS) could not make significant changes in MPV three groups.

Conclusion: The results showed that MPV on the first day was significantly higher in patients with sepsis or with sepsis and IVH.

Key words: Hemorrhage, Mean Platelet Volume, Newborn, Sepsis

Introduction

Intraventricular hemorraghe (IVH) is the most common intracerebral disorder in premature neonates. The prevalence of IVH in neonates with weight lower than 1500 g and less than 32 weeks of gestational age is 15% (1-3). The best screening method is cranial ultrasound which is usually performed at 3–7 days after birth (4-7). The early prevention and treatment of IVH – induced neurological complications will require the determination of IVH –related risk factors (8). Until recently, several agents have been evaluated in terms of IVH incidence in premature neonates such as low gestational age and prematurity, low birth weight, prolonged mechanical ventilation, mother treating with sulfate magnesium, hyaline membrane disease, hypercapnia, lower Apgar score at 5 minutes, pneumothorax, natural delivery, ischemia, increased or decreased blood pressure, high venous pressure, and hypovolemia (9,10). In recent years, various studies have been conducted on the association of peripheral blood platelet index with IVH incidence in premature neonates. One of the important parameters is mean platelet volume (MPV) which is in the range of 7 to 9 fl (11). Based on Wasiluk et al.'s study (2009), platelet count in preterm neonates was significantly low but MPV was equivalent (12). The results on the correlation between MPV and IVH are controversial, some reported the

correlation of high MPV and IVH but others could not demonstrate such a relation (13-15).

Among the other significant factors that guide prompt intervention for IVH, platelet count (PLT) and other platelet parameters have been insufficiently evaluated. All the previously identified risk factors seem to induce IVH, but thrombocytopenia seems to contribute to IVH by causing haemostatic failure. However, guidelines for the prevention of IVH in the neonatal period have remained an issue of strong controversial debate. On the basis of the pathophysiology of IVH, few studies have attempted to justify the administration of several factors that target mainly the coagulation cascade. Most importantly, there is limited evidence on platelet transfusion guidance in premature infants. Although there is no evidence about the relationship between PLT and the occurrence of major hemorrhage, preterm infants are commonly transfused prophylactically when PLT falls below an arbitrary limit, and this threshold is usually higher than that of older infants or adults. The optimal use of PLT transfusions in high risk premature neonates is yet to be defined.

The aim of the present study was to determine the relationship between MPV on the first to third days of birth with IVH and sepsis in premature neonates admitted into neonate's intensive care unit (NICU).

Materials and Methods

This case – control study was conducted on 60 premature neonates who were admitted to Tehran Bahrami Hospital NICU in 2015., After obtaining informed consent from parents, the neonates were categorized in three groups of sepsis, IVH and sepsis, no IVH and sepsis. There were 20 patients in each group. The first two groups were considered as the case groups and the latter as the control group. In this study, the sample size was estimated according to Cekmez et al.,'s study (16). This study was intiated after being approved by the Ethics Committee of Tehran University of Medical Sciences(Code of Ethics:1384-05-43-4126). The inclusion criteria included prematurity (gestational age lower than 37 weeks), IVH based on transcranial ultrasonographic criteria (Papile Classification System), and blood infection. Patients with mother's severe preeclampsia, diabetes mellitus, uterine infections (chorioamnionitis) and anti-convulsive drugs consumption history or the presence of thrombocytopenia, congenital malformations, fetal hydropse and metabolic disorders were excluded from the study. Neonatal data, including gender, birth weight, Apgar score at 5 minutes, type of delivery, presence of respiratory distress syndrome (RDS) or sepsis, type of accounting organism, platelet coun,t and MPV on the first and third days of birth as well as mothers data, including gestational age and prenatal steroids administrationwere recorded in check lists. IVH was graded as 1 to 4 based on the Papile Classification System. After data collection, analysis was performed using SPSS (version 21). Continuous variables were expressed as mean ± standard deviation; whereas, categorical variables were expressed as numbers with percentages and were compared between 2 groups using Student's t-test and ANOVA test for continuous variables and chi-square test was run for categorical variables. The significance level was set at $P<0.05$.

Results

In this retrospective case control study, the infants were matched into two groups based on age, sex and type of delivery. Ten (10) newborns (50%) of the sepsis group (case group) and 13 newborns (65%) of the IVH – sepsis group, and 10 newborns (50%) of the control group were male ($P = 0.523$). Seven cases (35%) with IVH grade four, seven cases with IVH grade two, five cases (25%) with IVH grade three, and one case (5%) with IVH grade one were

observed (Table I). Two newborns of each group (3.3%) died (P- value = 0.04). Most deliveries were by cesarean section. Eleven (11) neonates (55%) of the IVH and sepsis group had Apgar score lower than five. Fourteen (14) neonates (70%) of the IVH and sepsis group and 8 newborns (40%) of the sepsis group suffered from RDS. Platelet counts and MPV are presented in Table II. Considering MPV on the first and third days, no significant statistical correlation was found among three groups. The MPV of the first day was significantly lower in the case group than that of two other groups (P- value = 0.004) but no relation was discovered with respect to MPV on the third day. The MPV and platelet volume on the first and third days are listed in Table III. The relationship between sex (Table 4) and other variables (Table 5) and RDS (Table 6) have been shown.

Table I: Gestational age, birth weight and onset time of sepsis in studied groups

Variables	Group	Mean ± SD	P- value
Gestational age	sepsis	33.4±3.06	<0.001
	IVH and sepsis	31.3±3.02	
	control	36.2±0.61	
Birth weight	sepsis	2108.25±671.62	<0.001
	IVH and sepsis	1877.25±651.87	
	control	2917.5±347.54	
Onset time of sepsis	sepsis	12.4±12.66	0.3
	IVH and sepsis	9.31±8.70	

TableII: Outcomes, type of delivery, Apgar score at 5 minute and incidence of RDS in studied groups

		Sepsisgroup		IVH+ Sepsisgroup		Control group		
	Variables	Frequency	Percent	Frequency	Percent	Frequency	Percent	P- Value*
Outcome	Discharge	17	85	12	60	20	100	0.04
	expired	2	3.3	2	3.3	0	0	
	Transfer to another hospital	0	0	2	3.3	0	0	
	Personal satisfaction	1	1.7	4	6.7	0	0	
Type of delivery	C/S	13	65	18	90	15	75	0.1
	NVD	7	35	2	10	5	25	
Apgar at minute 5	<5	4	20	11	55	0	0	<0.01
	6-7	2	10	6	30	0	0	
	8-9	14	70	3	15	20	100	
RDS	Yes	8	40	14	70	0	0	<0.001
	No	**12**	**60**	**6**	**30**	**20**	**100**	

C/S: Caesarean section; NVD: Naturally Vaginal Delivery; RDS: Respiratory Distress Syndrome; IVH: Intraventricular hemorrhage

Table III: The mean platelet count and MPV at first and third days in studied groups

Variables	Group	Mean	±SD	P- value*
Platelet count at first day	sepsis	236550	117456.58	0.2
	IVH and sepsis	292950	116650.38	
	control	262050	104501.05	
Platelet count at first day	sepsis	236550	117456.58	0.5
	IVH + sepsis	292950	116650.38	
Platelet count at third day	sepsis	244700	88551.56	0.5
	IVH + sepsis	251600	106714.27	
MPV at first day	sepsis	10.66	1.28	0.004
	IVH + sepsis	10.65	1.19	
	control	8.61	0.69	
MPV at first day	sepsis	10.66	1.28	0.4
	IVH + sepsis	10.65	1.19	
MPV at third day	sepsis	11.22	1.31	0.7
	IVH + sepsis	11.22	1.40	

MPV: Mean platelet volume

Table IV: The association between gender and platelet volume and count

	Female	**Male**		
P- Value*	Mean± SD	Mean± SD	Group	Variables
0.084	294800±105776	178300±101961	Sepsis	Platelet
0.077	360285±131234	256692±94151	IVH + Sepsis	count
0.693	273800±80924	250300±127274	control	
0.125	10.28±1.52	11.01±0.98	Sepsis	MPV
0.379	10.32±0.9	10.83±1.32	IVH + Sepsis	
0.293	8.78±0.48	8.44±0.85	Control	

IVH: Intraventricular hemorrhage

TableV: The association between birth weight, gestational age and time onset of sepsis with platelet volume and counts

		Birth weight		Gestational age		Time onset of sepsis	
	Group	Pearson coefficient	P- value	Pearson coefficient	P- value	Pearson coefficient	P- value
Platelets count	Sepsis+IVH	0.162	0.494	0.173	0.466	-0.063	0.798
	Sepsis	-0.215	0.362	-0.222	0.347	-0.171	0.472
	Control	0.021	0.929	0.437	0.054	----	----
MPV	Sepsis+IVH	-0.005	0.985	-0.003	0.989	-0.096	0.696
	Sepsis	-0.332	0.165	-0.372	0.172	0.122	0.618
	Control	0.217	0.357	0.130	0.585	----	----

IVH: Intraventricular hemorrhage; MPV: Mean platelet volume

Table VI: The association of RDS and platelet count and MPV

		Presence of RDS	**Absence of RDS**	
	Group	**Mean± SD**	**Mean± SD**	**P- Value**
Platelets count	Sepsis+IVH	282285±100459	317833±15622	0.526
	Sepsis	284500±1135331	204583±113314	0.193
MPV	Sepsis+IVH	10.63±0.89	10.70±0.89	0.908
	Sepsis	10.77±1.62	10.59±1.05	0.744

IVH: Intraventricular hemorrhage; MPV: Mean platelet volume

Discussion

Despite the increasing survival rate of premature infants during recent decades, IVH is still one of the major causes of neurologic developmental problems (17-19). Many studies have suggested that MPV can predict the development of some diseases such as RDS, IVH, necrotizing enterocolitis, and sepsis in preterm newborns (20-22). The present study showed that the MPV value in the healthy group was significantly lower than the two other groups. MPV and platelet count had no relationship with gender, birth weight, gestational age, sepsis onset, and the incidence of RDS. In their study, Hussein et al. demonstrated that the MPV value in newborn with bronchopulmonary dysplasia (BPD) (12.3 fl) and neonate with intraventricular hemorrhage (IVH) (11.6 fl) was higher in the control group (9.6 fl) but the platelet count was the same among groups but the MPV value in neonates with RDS was higher than others(11). Dani et al., reported that MPV at birth time was the same in 3 groups of preterm neonates with IVH, BPD and control group but over 24 to 48 h after birth in neonates with BPD (13). The MPV value was higher than the control group (e.g. MPV > 11 fl can increase risk of BPD) but MPV in newborns with intraventricular hemorrhage had no difference with the control group. Canpolat et al., reported high MPV in premature infants with RDS (23).Cekmez et al., reported that the measured MPV at birth time among neonates with and without sepsis and cases with and without ROP (16) was the same. The MPV value was higher in newborns with BPD, NEC, and IVH in comparison with the control group. In Kim et al.'s study, increase in MPV was associated with the mortality of patients with severe sepsis(24). Prolonged infection and death is associated with high MPV value. Charoo et al.,reported that increased duration of sepsis could decrease platelet count and birth weight, especially in premature neonates and neonates with low birth weight (25). Decreased platelet count is directly associated with necrotizing entrocolitis and disseminated intravascular coagulation. Tasyurt et al., showed that the MPV of the sepsis group was significantly lower; however, the MPV and PCT of the sepsis group was higher than the control group (26(.von Vietinghoff et al., considered the male gender, birth weight < 1250 gr, and the 5th minute Apgar score < 8 as other independent risk factors of IVH(27).

Larkinand et al., (28) showed that the development of thrombocytopenia; either a relative or an absolute decrease, during a septic episode was a significant event, associated with doubling of the expected mortality rate from that episode. The exact mechanism underlying sepsis-associated thrombocytopenia remains unclear and it may be that it is a multifactorial phenomenon. Should a distinct or dominant pathway emerge in this process, it is probable that this would be a potential therapeutic target. Correlation between high MPV and inflammatory events especially sepsis (29) and IVH (30) were observed. Infection and IVH can result in an increase in platelet count and volume which is in line with this study. However, in terms of platelet count, the results have been contrary with many other studies.

Conclusion

The result of this study showed that the MPV value on the first day was significantly higher in patients with sepsis or with IVH and sepsis. Gestational age and birth weight were significantly lower in IVH and sepsis group. Accordingly, we can conclude that these indices can be used as measurements for predicting the risk of IVH and sepsis in premature newborns; however, by identification of premature newborn with IVH and sepsis that is at

risk, measures can be taken for the reduction of mortality and morbidity.

Conflict of interest

There is no conflict of interest to declare.

References

1. Behrman R, Klieghman R, Jenson H. Nelson's Textbook of Pediatrics. 17th Ed. Saunders. Philadelphia. 2004.
2. Hallevi H, Albright KC, Aronowski J. Intraventricular hemorrhage: Anatomic relationships and clinical implications. Neurology 2008;70(11):848-852.
3. Bajwa NM, Berner M, Worley S, Pfister RE. Population based age stratified morbidities of premature infants in Switzerland. Swiss Med Wkly 2011; 24; 141: 13212-13216.
4. Ballabh P. Intraventricular Hemorrhage in Premature Infants: Mechanism of Disease. *Pediatric res* 2010; 67(1):1-8.
5. McMillan JA, Feigin RD. Oski's Pediatrics. 4th ed. Washington. lippincottwiliams. 2006.
6. Whitaker AH, Feldman JF, Van Rossem R, Schonfeld IS, Pinto-Martin JA, Torre C, et al. Neonatal cranial ultrasound abnormalities in low birth weight infants: relation to cognitive outcomes at six years of age. Pediatrics 1996; 98(4):719-729.
7. Pinto-Martin JA, Riolo S, Cnaan A, Holzman C, Susser MW, Paneth N. Cranial ultrasound prediction of disabling and nondisabling cerebral palsy at age two in a low birth weight population. Pediatrics. 1995; 95(2):249-254.
8. Saki MR. Intraventricular Hemorrhage in Premature Infants and Its Association with Pneumothorax. Acta Med Iran 2012; 50(7):473-476.
9. Wells JT, Ment LR. Prevention of intraventricular hemorrhage in preterminfants. Early Hum Dev 1995; 42(3):209-233.
10. Vohr B, Ment L. Intraventricular hemorrhage in the preterm infant. Early Hum Dev 1996; 44(1):1-16.
11. Hussein NF, Helaly NSE, Ghanya EAA, Anisb SK. Relationship between Mean Platelet Volumeand Bronchopulmonary Dysplasia and Intraventricular Hemorrhage in Very Low Birth Weight Neonates. J American Sci 2012; 8(5): 554-650.
12. Wasiluk A, Osada J, Dąbrowska M, Szczepański M, Jasinska E. Does prematurity affect platelet indices? Adv Med Sci 2009;54(2): 253-235.
13. Dani C, Poggi C, Barp J, Berti E, Fontanelli G. Mean platelet volume and risk of bronchopulmonary dysplasia and intraventricular hemorrhage in extremely preterm infants. Am J Perinatol 2011;28(7):551-556.
14. Setzer ES, Webb IB, Wassenaar JW, Reeder JD, Mehta PS, Eitzman DV. Platelet dysfunction and coagulopathy in intraventricular hemorrhage in the premature infant. J Pediatr 1992;100(4):599-605.
15. Bhat RY. Platelet indices in neonatal sepsis: A review. World J Clin Infect Dis 2017; 7(1): 6-10.
16. Cekmez F, Tanju IA, Canpolat FE, Aydinoz S, Aydemir G, Karademir F, et al. Mean platelet volume in very preterm infants: a predictor of morbidities? Eur Rev Med Pharmacol Sci 2013;17(1):134-137.
17. Vela-Huerta MM, Amador-Licona M, Medina-Ovando N, Aldana-Valenzuela C. Factors associated with early severe intraventricular haemorrhage in very low birth weight infants. Neuropediatrics 2009; 40(5): 224-227.
18. Ancel PY, Livinec F, Larroque B, Marret S, Arnaud C, Pierrat V, et al. Cerebral palsy among very preterm children in relation to gestational age and neonatal ultrasound abnormalities: the EPIPAGE cohort study. Pediatrics 2006; 117(3): 828-835.
19. Patra K, Wilson-Costello D, Taylor HG, Mercuri-Minich N, Hack M. Grades I-II intraventricular hemorrhage in extremely low birth weight infants: effects

on neurodevelopment. J Pediatr 2006; 149(2): 169-173.
20. Bolouki Moghaddam K, Zarkesh M, Kamali A, Dalili S, Heidarzadeh A, Hassanzadeh Rad A. The Association of Mean Platelet Volume with Intra Ventricular Hemorrhage and Broncho Pulmonary Dysplasia in Preterm Infants. IJPHO 2015; 5(4):227-232.
21. Oncel MY, Ozdemir R, Yurttutan S, Canpolat FE, Erdeve O, Oguz SS, et al. Mean platelet volume in neonatal sepsis. J Clin Lab Anal 2012; 26(6):493-496.
22. Nourripoor S, Tabasizadeh H, Afjehi A, Ghorbani R, Seifhashemi M, Masoudian N. Could mean platelet volume predict developing of bronchopulmonary dysplasia in preterm infants with respiratory distress syndrome. Iranian J Neona 2013;4(3):35–41.
23. Canpolat FE, Yurdaködk M, Armangil D, Yiğit Ş. Mean platelet volume in neonatal respiratory distress syndrome. Pediatr Int 2009;51(2):314–316.
24. Kim CH, Kim SJ, Lee MJ. An Increase in Mean Platelet Volume from Baseline Is Associated with Mortality in Patients with Severe Sepsis or Septic Shock. PLoS ONE 2015;10(3):0119437-0119445.
25. Charoo BA, Iqbal J, Iqbal Q, Mushtaq S, Bhat AW. Nosocomial sepsis-induced late onset thrombocytopenia in a neonatal tertiary care unit: a prospective study. Hematol Oncol Stem Cell Ther 2009;2(2):349-353.
26. Taşyurt N, Olukman Ö, Çalkavur S, Atlıhan F, Kılıç F, Genel F, et al. Diagnostic value of platelet parameters in neonatal sepsis. Behcet Uz Cocuk Hast Derg 2012; 2(1):7-10.
27. von Vietinghoff S, Ley K. Interleukin 17 in vascular inflammation. Cytokine Growth Factor Rev 2010; 21(6): 463-469.
28. Larkin CM, Santos-Martinez MJ, Ryan T, Radomski MW. Sepsis-associated thrombocytopenia. Thromb Res 2016;141:11-16.
29. Aydin B, Dilli D, Zenciroglu A, Karadag N, Beken S, Okumus N. Mean platelet volume and uric acid levels in neonatal sepsis. Indian J Pediatr 2014; 81(12): 1342-1346.
30. Mosayebi Z, Sepidarkish M, Nikseresht Z, Sharifi M, Sagheb S, Nariman SH. Mean Platelet Volume as a Marker of Intraventricular Hemorrhage in Very Premature Infants. Iran J Pediatr 2017; 27(2): 8322-8333.