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Could mean platelet volume predict developing of bronchopulmonary dysplasia in preterm infants with respiratory distress syndrome?

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ABSTRACT

Background: some studies have suggested correlation between MPV index and inflammatory diseases such as rheumatoid arthritis in adults. Though bronchopulmonary dysplasia is also an inflammatory disease which develops in preterm neonates with Respiratory distress syndrome, we decided to study the possible correlation between the mean platelet volume (MPV) and the occurrence of bronchopulmonary dysplasia (BPD).

Methods: We reviewed the medical records of 280 infant with the diagnosis of RDS admitted to the neonatal intensive care unit of the Mahdieh obstetrics and gynecology Hospital of Tehran and Amir general Hospital of semnan from April 2008 to April 2012. Infants who have been expired before first month of life were excluded. Enrolled infants were divided into BPD and no-BPD groups (30 with and 250 without BPD). MPV was determined during first three days of life in all cases.

Results: MPV measured during first three days of life was significantly(p=0.017) higher in the BPD than in the no-BPD group (10.8-0.96 versus 9.65-0.91 fL)but Platelet count at the same time were similar in the BPD and no-BPD groups, and MPV increment was associated with BPD development risk((OR=1.6, 95%CI:1.08-2.38, p=0.019) .

Conclusion: We concluded that higher MPV in the first three days of life is a probable risk factor for the development of BPD in preterm infants with RDS. This might be attributed to the fact that high MPV could prone the neonate to inflammatory and oxidative lung damage.

Keywords: oxidative lung damage, supplemental oxygen therapy, neonatal intensive care unit, preterm neonates, Platelet

Introduction

Bronchopulmonary dysplasia (BPD) is an ominous complication of respiratory distress syndrome (RDS) which develops in preterm infants requiring ventilation and supplemental oxygen therapy[1].BPD was first described by Norway in 1967[2].BPD incidence is inversely related to gestational age. Clinically BPD is defined as dependency to supplemental oxygen at 36 week of postconceptional age[1].Pathogenesis of BPD is multifactorial. Atelectotrauma due to surfactant deficiency and ventilator induced volutrauma promote injury to lung[1]. Oxygen free radicals that cannot be neutralized by immature antioxidant system of the pretermInfant deteriorate lung damage. Since deposits of fibrin are seen in alveolar spaces in hystopathologic evaluation of sever RDS, the role of coagulation system in promoting BPD is probable[3], and since inflammatory mediators and cells have been detected in bronchoalveolar lavage aspirates of preterm infants with BPD[1], inflammatory system is also engaged in pathogenesis of BPD. Platelet has an important role in both coagulation and inflammatory systems. Some studies have shown that larger platelets are more active due to more cytoplasmic granules they have[4]. Some studies have demonstrated correlation between disease activity and complications with higher MPV in inflammatory diseases such as infective

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endocarditis[5] and rheumatoid arthritis[6] in adults. However, MPV has been poorly investigated in preterm infants. Only one study by Dani et al showed that MPV measured at 24 to 48 hours of life was higher in the BPD than in the no-BPD preterm infants with RDS[3]. In this study we hypothesized that preterm infants who have higher MPV during first three days of life are at an increased risk of developing BPD. If we could predict BPD promotion in preterm infants with RDS this may be possible to interrupt this catastrophic process by preventive measures such as weaning of ventilator more rapid and use of minimal oxygen concentrations.

Material and Method

We have reviewed the medical sheets of 280 preterm infants with RDS diagnosis admitted to neonatal intensive care unit of the Mahdieh Obstetrics and Gynecology Hospital of Tehran and Amir general hospital of Semnan, Iran from April 2008 to April 2012.Inclusion criteria was admission by RDS diagnosis. Infants who died before 28 days of life were excluded from study.30 infants with RDS were complicated by BPD but 250 infants didn't progress to BPD. Following information were registered for all infants: Birth weight, gender, gestational age, hospitalization duration, Apgar score at 1st and 5th minutes of birth, rout of delivery, Intrauterine growth retardation, cardiopulmonary resuscitation in delivery room, surfactant need, ventilation mode and duration, complications occurred during admission including intraventricular hemorrhage(IVH), pneumothorax, necroziting entrocolitis(NEC), patent ductus arteriosus(PDA) and history of gestational hypertension,(GHTN) gestational diabetes mellitus(GDM) and premature rupture of membranes(PROM)>18 hours in mother.MPV and platelet count was determined in all infants in the first three days of life by obtaining 2 milliliters of Blood for complete count by venipuncture for this purpose. Coulter counter model ABx micros 60 Cell was used for MPV and platelet measurement .Diagnosis of RDS was made by clinical symptoms including tachypnea, grunting, intercostal and subcostal retraction, nasal flaring, cyanosis, and chest x ray findings including fine reticular granularity pattern and air bronchogaram[1].Diagnosis of BPD was established if infant was oxygen dependent at 36 week of postconceptional age[1].In this study MPV which was determined during first three days of life was compared between preterm infants with RDS who developed in to BPD (BPD group, n=30)and who didn't progressed in to this complication(no-BPD group, n=250).

All statistical analysis were carried out using SPSS for Windows version 16.0 (SPSS, Chicago,IL, USA). Univariate statistical analysis was performed using the Student t test and mann-whitney for parametric continuous variables, and κ^2 test for non parametric variables. A $p < 0.05$ was considered statistically significant. In order to assess the effect of MPV in predicting BPD, logistic regression analysis was used. Effect estimates are expressed as odd ratio with profile likelihood-based 95% confidence limits.

Results of analysis of infant's characteristics were described by mean values and standard deviation.

This study has obtained ethical approval from the ethics committee of Semnan University of Medical Sciences.

Results

In our study 280 preterm infants with RDS diagnosis were enrolled.30 infants (10.7%) developed in to BPD (BPD group) and the other 250 infants(89.3%) didn't progress in to BPD(no-BPD group).

BPD group had lower GA, birth weight, Apgar score at 1st and 5th minutes of life, as well as higher history of resuscitation in delivery room, need for surfactant therapy, ventilator dependency ,and more complications including IVH, NEC, pneumothorax and pulmonary hemorrhage, but there was not any statistically significant difference in infants gender ,mode of delivery, history of GHTN, GDM, PROM>18 hours and antenatal bethametasone administration and the rate of PDA between two groups.

MPV measured during the first three days of life was significantly higher in the BPD group than in the no-BPD group (10.08_0.96versus 9.65_0.91 fL, p=0.033;) but platelet count measured at the same time didn't show any statistically significant difference.(Table 1).

Results are mean_standard deviation, or n (%.).little figures are MIN –MAX of data . (A)IUGR ,intra uterine growth retardation;(B) GDM ,gestational diabetes mellitus;(C) GHTN ,gestational hypertension;(D) NEC ,necroziting entrocolitis;(E) IVH, intraventricular hemorrhage;(F) PDA, patent ductus arteriosus;(G) PROM, premature rupture of membranes;(H) SIMV, synchronized intermittent mandatory ventilation;(I) CPAP, continuous positive airway pressure;(J) MPV, mean platelet volume; (K)BPD,

bronchopulmonary dysplasia; (L) fl, femtolitre ;(M) dl, decilitre;

logestic Regression analysis demonstrated that higher MPV during the first 72 hours of birth can predict the development of BPD in preterm infants who suffered from RDS (OR=1.6, 95%CI:1.08-2.38, p=0.019).

Discussion

Our study is one of the first researches that investigates the correlation between MPV and BPD in preterm infants with RDS. Our results showed that higher MPV during first three days of life is associated with higher risk of progression in to BPD in preterm infants with RDS, and infants in BPD group had lower birth weight, GA , Apgar score at 1 and 5 minutes of birth and more surfactant and ventilatory supports than no-BPD group infants. But there was not any difference in platelet count between two groups. These findings are consistent with the study results performed by Dani et al In Italy[3] and also Nouran[4] et al in Egypt who demonstrated MPV was significantly higher in BPD than no-BPD group(12.3±1.4 vs 9.6±1.2 fl, p=0.001)in the first 24-48 hours of life. As Also in a study performed by Cekmez[5] et al in Turkey MPV in the first day of life was higher in infants with BPD(9.8±1.3 vs 7.06±0.6)than in the control group.

Complications occurred during admission including IVH, NEC, pulmonary hemorrhage and pneumothorax were also higher in the BPD group. This may be due to characteristics of BPD group such as lower birth weight, GA, and more severe RDS requiring more interventional modalities such as ventilatory support and surfactant administration ,and finally common underlying inflammatory pathogenesis of this complications with BPD that make BPD group susceptible to this complications. Higher MPV during first three days of life in BPD group confirms previous studies which showed correspondence of higher MPV with disease activity and complications in rheumatoid arthritis and infective endocarditis in adults[7,8]and correlation between higher MPV and severe RDS [9]and BPD development [3]in preterm infants.

larger platelets are more reactive due to containing more preinflammatory and precoagulative granules they have[6].In the BPD pathogenesis alveolocapillary damage following oxygen free radicals exposure and ventilatory volutrauma induces an increased level of plasminogen activator inhibitor-1 which promotes platelet aggregation and activation[10,11].

The final outcome of disruption of the alveolocapillary membrane integrity in RDS is a greater leakage of coagulative factors into the alveolar space and more alveolar fibrin deposition and hyaline membrane formation in preterm infants with the higher MPV. As fibrinogen and derivatives are potent inhibitors of surfactant [12,13],Therefore high MPV during first three days of life may promote BPD development by worsening RDS through surfactant inhibition and increased mechanical ventilation and oxygen requirements, which in a viscous cycle leads to more inflammatory cells and platelet recruitment and eventually more fibrin depositions and destroying lung tissue by these cells and establishing BPD[14,15].

The limitations of our study were small size of BPD group and inability to evaluate other possible factors influencing MPV and BPD correlation and finally not following up further MPV changes after three days of birth. We suggest performing further studies with larger BPD group and purposing other possible factors that predispose infants to BPD and serial MPV measurements after three days of life. If future studies could confirm our results, MPV might be used as an early inexpensive and simple measurable predicting marker for BPD development in preterm infants with RDS that makes the opportunity for right time intervention by measures such as using minimal oxygen concentration, weaning off ventilator as fast as possible and using medications (corticosteroid).

Conclusion

We concluded that higher MPV in the first three days of life is a probable risk factor for the development of BPD in preterm infants with RDS. This might be because high MPV could favor inflammatory and oxidative lung damage.

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Table1. Clinical Characteristics, Complication Rates, and Platelet Count and Volume in Infants with or without BPD

	BPD[K](n=30)	No BPD(n=250)	P
Birth weight(gram)	1044(199.40)	1787(579.92)	<0.001
Male gender	16 (53.3%)	146(58.4%)	0.595
Gestational age(week)	28.27(1.57)	32.31(2.47)	<0.001
Cesarian section	26(86.7%)	211(84.4%)	0.745
Multiparity	6(20%)	93(37.2%)	0.063
Multi fetal Pregnancy	13(43.3%)	95(38%)	0.571
hospitalization duration (day)	56.60(21.31)	18.86(15.88)	<0.001
Apgar score at 1 min	6.27(1.76)	7.79(1.29)	<0.001
Apgar score at 5 min	7.70(1.62)	9.06(0.93)	<0.001
Resuscitation in delivery room	21(70%)	78(28.4%)	<0.001
IUGR[A]	5(16.7%)	13(5.2%)	0.001
GDM[B]	2(6.7%)	22(8.8%)	0.693
GHTN[C]	5(16.7%)	33(13.2%)	0.6
NEC[D]	8(26.7%)	15(6.0%)	<0.001
IVH[E]	15(50%)	38(15.2%)	<0.001
PDA[F]	6(20.0%)	81(32.4%)	0.166
Pulmonary hemorrhage	6(20.0%)	1(0.4%)	<0.001
Pneumothorax	8(26.7%)	7(2.8%)	<0.001
PROM[G]>18 hours	2(6.7%)	22(8.8%)	0.693
Antenatal bethametason	10(33.3%)	24(9.6%)	0.005
Surfactant administration	29(96.7%)	124(49.6%)	<0.001
SIMV[H] need	30(100%)	82(32.8%)	<0.001
SIMV duration	33.20(20.88)	1.56(3.50)	<0.001
CPAP[I] need	26(86.7%)	108(43.2%)	<0.001
CPAP duration	8.87(8.42)	1.32(2.70)	<0.001
MPV[J](fl[L])	10.08 (0.96)	9.65(0.91)	0.017
Platelet count(×1000.dl[M])	(77.94)207.40	226.22(67.97)	0.297

Result are mean standard deviation, or n (%.).BPD, bnronchopulmonary dysplasia, IVH, interaventricular Hemorrhage, MPV, mean plateletvolume, PDA, patent ductus arteriosus, SIMV, synchronized intermittent mandatory ventilation,CPAP,continuous positive airway pressure,PROM.premature rupture,of membranes,dl.decilitre,fl,femtolitre