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Original Article

The relationship between thrombocytopenia and intraventricular hemorrhage in neonates with gestational age <35 weeks

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Abstract

Background The prevalence of thrombocytopenia in neonates ranges from 22 to 35%, and one of the most feared complications is intraventricular hemorrhage (IVH). Previous research in Cipto Mangunkusumo Hospital (CMH), Jakarta reported a high incidence of IVH (43.47%) in infants with a gestational age of <35 weeks. Intraventricular hemorrhage causes disturbances in neurological development and can be fatal. In Indonesia, research on the relationship between thrombocytopenia and IVH has been limited.

Objective To study the relationship between thrombocytopenia and IVH in neonates with gestational age <35 weeks and assess for a correlation between the severity of thrombocytopenia and the severity of IVH.

Methods This cross-sectional study was performed by reviewing medical records in the Neonatology Division of the Child Health Department, University of Indonesia, CMH. Subjects were neonates hospitalized from January 2012 to December 2014 with IVH. Subjects were categorized into either mild to moderate IVH (grade ≤2) or severe IVH (grade >2). Thrombocyte counts were recorded on the same day as the diagnosis of IVH.

Results The risk of severe IVH was 28.2% in neonates with thrombocyte counts <100,000/uL, and 10.4% in neonates without thrombocytopenia (P=0.014). Multivariate analysis revealed that gestational age <32 weeks and the use of respiratory support (ventilator and high frequency oscillatory ventilation) had significant associations with severe IVH. However, multivariate analysis did not show a significant relationship between thrombocytopenia and severe IVH (correlation coefficient = 0.21).

Conclusion Thrombocytopenia is not significantly associated with the incidence of severe IVH based on multivariate analysis. Also, the severity of thrombocytopenia has no correlation with the severity of IVH. **[Paediatr Indones. 2016;56:242-50. doi: 10.14238/pi56.4.2016.242-50]**.

Keywords: *gestational age <35 weeks; intraventricular hemorrhage; thrombocytopenia.*

The prevalence of thrombocytopenia in neonates varies between 1 to 5% and it is reportedly more frequent in neonates treated in the intensive care unit, at 22 to 35%. Thrombocytopenia is one of the main risk factors for intraventricular hemorrhage (IVH).[1] In neonates with thrombocytopenia, the main focus is to prevent the occurrence of major hemorrhage, including IVH, since IVH affects neurological development and may be fatal, especially in severe

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IVH.[1,2] Some studies showed a strong relationship between thrombocytopenia and IVH, but others found no relationship, or a relationship between only severe thrombocytopenia and IVH.[1,4,5] Studies on the severity of thrombocytopenia and the risk of IVH in neonates have been limited and reported differing results.[6-10]

In Indonesia, no studies have been done on thrombocytopenia and IVH. The incidence of thrombocytopenia in neonates was 12.1% in Cipto Mangunkusumo Hospital (CMH).[11] Another study in CMH found that the incidence of IVH in neonates with gestational age <35 weeks was 43.47%, of which 7.6% had severe IVH, but it had no analysis of thrombocytopenia as a potential factor contributing to the occurrence of IVH.[12] The high incidence of IVH highlights the urgency of this study to assess for a relationship between thrombocytopenia and IVH in neonates with gestational age <35 weeks.

The aims of this tudy were to study the relationship between thrombocytopenia and IVH in neonates with gestational age <35 weeks, and assess for a correlation between the severity of thrombocytopenia and the severity of IVH.

Methods

A cross-sectional, descriptive study was performed in neonates with gestational age <35 weeks and IVH who were treated at the Division of Neonatology, CMH, from January 2012 to December 2014. We excluded neonates with head trauma, incomplete baseline medical records (sex, gestational age, birth weight, Apgar scores, or mode of delivery), or no platelet data on ± 2 days of their cranial ultrasound results.

Subjects data were collected from the medical records. Reviews of cranial ultrasound and patient medical records that fulfilled the inclusion criteria were carried out within the last 3 years, retrospectively. We recorded the presence of IVH as detected by cranial ultrasound, and classified subjects according to Volpe criteria.[3] Data for demographics and clinical conditions of all infants were collected, including gender, gestational age, birth weight, mode of delivery, asphyxia status [criteria of the American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologyst (ACOG)], a history of manual positive pressure ventilation (PPV), or other use of respiratory support, sepsis, fluctuations in blood pressure, hypotension, and other simultaneous hemorrhage at the time of IVH diagnosis.

Platelets count, from within 2 days before or after the patient was diagnosed with IVH, were recorded. Moreover, prothrombin time (PT) and activated partial thromboplastin time (aPTT) levels were recorded. Thrombocytopenia was defined to be a thrombocyte count less than 150,000/uL, and divided into categories of mild (100,000 - <150,000/uL), moderate (50,000 - <100,000/uL), severe (30,000 - <50,000/uL), and very severe (<30,000/uL).[1] Sepsis was defined to be a collection of systemic clinical symptoms, along with bacteremia occurring in the first month of life, regardless of blood culture examination results.[13,14] Hypotension was defined to be blood pressure of more than 2 standard deviations below normal values according to gestational age.[15] Blood pressure fluctuation was defined to be a significant and continuous change in systolic and diastolic blood pressure with a coefficient of variation of >10%.[3] If cranial ultrasounds in one baby had differing results, the most severe one was taken. Subjects were classified based on the degree of IVH (1-4), then they were classified into two groups, either mild to moderate IVH (≤2) or severe IVH (>2). This study was approved by the Research Ethics Committee of FKUI-CMH.

Results

Based on cranial ultrasounds, 260 subjects had varying degrees of IVH. However, there medical records for 133 patients had incomplete information and 11 patients did not meet the inclusion criteria. Therefore, the analysis included only 116 subjects.

In our sample, there were more males than females (male: female ratio of 1.42:1). Subjects' gestational ages were mostly between 32 – 34 weeks (50%), with a median of 31.5 (24-34) weeks. The median birth weight was 1,325 (580 – 2,455) g. Only 56 of 116 (48.3%) subjects were examined for PT and aPTT, as shown in **Table 1**. In addition, blood pressure examinations were done in only 24 of 116 (20.7%) subjects, as we had a limited number of appropriately-

sized sphygmomanomters. The most common type of IVH in our 116 subjects was IVH grade 1, seen in 87 subjects (75%). IVH grade 2 was found in 10 subjects (8.6%), IVH grade 3 in 8 subjects (6.9%), and IVH grade 4 in 11 (9.5%) subjects. Thirty-seven subjects (31.9%) suffered from IVH in the first week (19.8% occurring on the third day), and 60 subjects (52.7%) did not have thrombocytopenia.

The characteristics of subjects in the IVH grade ≤2 and >2 groups are shown in **Table 1**. Subjects median platelets counts for IVH grade ≤2 was 185,000 (range 5,000-685,000)/uL, while that for IVH >2 was

Table 1. Characteristics of subjects

Characteristics	IVH grade ≤ 2 (n = 97)	IVH grade > 2 (n = 19)
Gender, n (%)		
Male	53 (54.6)	78.9)
Female	44 (45.4)	4 (21.1)
Gestational age, n (%)		
32-34 weeks	56 (57.7)	(10.5)
27-31 weeks	35 (36.1)	78.9)
< 27 weeks	6 (6.2)	2 (10.5)
Birth weight, n (%)		
> 1,500 g	42 (43.3)	(15.8)
1,000 – 1,500 g	39 (40.2)	(47.4)
< 1,000 g	16 (16.5)	7 (36.8)
Mode of delivery, n (%)		
Vaginal	37 (38.1)	(42.1)
≤ 1,500 g	24 (24.7)	(36.8)
> 1,500 g	13 (13.4)	(5.3)
Caesarian section	60 (61.9)	11 (57.9)
Asphyxia, n (%)		
No	97 (100)	100)
Yes	0 (0)	0 (0)
History of manual PPV, n (%)		
No	90 (92.8)	89.5)
Yes	7 (7.2)	2 (10.5)
Respiratory support, n (%)		
No	35 (36.1)	(0.0)
CPAP	34 (35.1)	(21.1)
Ventilator	27 (27.8)	57.9)
HFOV	1 (1.0)	4 (21.1)
Sepsis, n (%)		
Proven	30 (30.9)	(15.8)
Unproven	50 (51.5)	84.2)
No sepsis	17 (17.5)	0 (0)
PT or aPTT (n = 56), (x normal value), n (%)		
> 2x	12 (30.8)	(41.2)
≤ 2x	27 (69.2)	10 (58.8)
Hypotension (n = 24), n (%)		
Yes	6 (42.9)	(50)
No	8 (57.1)	5 (50)
Blood pressure fluctuation (n = 24), n (%)		
Yes	13 (92.9)	(90)
No	1 (7.1)	1 (10)
Thrombocytopenia, n (%)		
Yes	41 (42.3)	78.9)
Mild	13.4)	3 (21.1)
Moderate	12.4)	6 (31.6)
Severe	(7.2)	3 (10.5)
Very severe	9 (9.3)	3 (15.8)
No	56 (57.7)	4 (21.1)

77,000 (range 7,000-341,000)/uL. These differences were statistically significant (P=0.003).

Table 2 shows the bivariate analysis results between variables and IVH grades ≤2 and >2. Thrombocytopenia with platelets count <100,000/uL was significantly associated with IVH grade >2 (P<0.014). The incidence of IVH grade >2 with platelets count <100,000/uL was 11/39 (28.2%)

Table 2. Bivariate analysis of variables and IVH grade > 2

Variables	IVH grade ≤ 2 (n=97)	IVH grade > 2 (n=19)	OR	95% CI	P value
Gender, n (%)					
Male	53 (54.6)	15 (78.9)	3.113	0.963 to 10.062	0.049
Female	44 (45.4)	4 (21.1)			
Gestational age, n(%)					
< 32 weeks	41 (42.3)	17 (89.5)	11.610	2.540 to 53.058	0.000
≥ 32 weeks	56 (57.7)	2 (10.5)			
Birth weight, n (%)					
≤ 1500 g	55 (56.7)	16 (84.2)	4.073	1.113 to 14.897	0.024
> 1500 g	42 (43.3)	3 (15.8)			
Mode of delivery, n (%)					
Vaginal	37 (38.1)	8 (42.1)	1.179	0.434 to 3.201	0.746
Caesarian section	60 (61.9)	11 (57.9)			
Birth weight in vaginal delivery group, n (%)					
≤ 1500 g	24 (64.9)	7 (87.5)	3.792	0.420 to 34.265	0.402
> 1500 g	13 (35.1)	1 (12.5)			
Birth weight ≤ 1500 g, n (%)					
Vaginal delivery	24 (43.6)	7 (43.8)	1.005	0.327 to 3.086	0.000
Caesarian section	31 (56.4)	9 (56.2)			
Asphyxia, n (%)					
Yes	3 (3.1)	1 (5.3)	1.741	0.171 to 17.690	0.516
No	94 (96.9)	18 (94.7)			
History of manual PPV, n (%)					
Yes	7 (7.2)	2 (10.5)	1.513	0.289 to 7.914	0.640
No	90 (92.8)	17 (89.5)			
Respiratory support, n (%)					
Ventilator, HFOV	28 (28.9)	15 (78.9)	9.241	2.819 to 30.290	0.000
No, CPAP	69 (71.1)	4 (21.1)			
Sepsis					
Yes	80 (82.5)	19 (100)	-		0.071
No	17 (17.5)	0 (0)			
PT or aPTT (n = 56), (x normal value), n (%)					
> 2x	12 (30.8)	7 (41.2)	1.575	0.483 to 5.132	0.449
≤ 2x	27 (69.2)	10 (58.8)			
Hypotension					
Yes	6 (42.9)	5 (50)	1.333	0.261 to 6.805	1.000
No	8 (57.1)	5 (50)			
Blood pressure fluctuation (n = 24), n (%)					
Yes	13 (92.9)	9 (90)	0.692	0.038 to 12.572	1.000
No	1 (7.1)	1 (10)			
Platelets, n (%)					
< 100,000/uL	28 (28.9)	11 (57.9)	3.388	1.233 to 9.313	0.014
≥ 100,000/uL	69 (71.1)	8 (42.1)			

OR: odds ratio; 95%CI: 95% confidence interval

compared to 8/77 (10.4%) with platelets ≥100,000/uL. Multivariate analysis was done to further assess the relationships between variables with significant associations to IVH grade >2 on bivariate analysis (P<0.25). **Table 3** shows that gestational age <32 weeks and respiratory support (ventilator or HFOV) had significant associations with IVH grade >2. However, birth weight ≤1,500g and thrombocyte count <100,000/ul were not significantly associated with IVH grade >2, (P=0.454 and P=0.327, respectively). Logistic regression analysis revealed that IVH grade >2 was significantly associated with gestational age <32 weeks and the use of respiratory support, such as ventilator or HFOV (**Table 4**). Based on these results, subjects' with gestational age <32 weeks using a ventilator or HFOV had a 26.1% probability of having IVH grade >2, with a good area under curve (AUC) of 85.1%. To evaluate the relationship between degree of thrombocytopenia and degree of IVH, we determined the correlation coefficient, and found it to be 0.21 (P<0.05). This value indicates no correlation between the severity of IVH and the severity of thrombocytopenia.

Table 3. Multivariate analysis of variables and IVH grade >2

Variables	B	SE	OR	95% CI	P value
Male	1.035	0.663	2.814	0.767 to 10.328	0.119
Gestational age < 32 weeks	2.335	1.111	10.326	1.171 to 91.033	0.036
Birth weight ≤ 1,500 g	-0.805	1.073	0.447	0.055 to 3.667	0.454
Respiratory support (ventilator and HFOV)	1.798	0.674	6.040	1.613 to 22.619	0.008
Platelets count < 100,000/uL	0.589	0.601	1.802	0.555 to 5.850	0.327

B: constant, SE: standard error

Table 4. Logistic regression analysis of risk factors variables for IVH grade > 2

Variables	B	SE	OR	95% CI	P value
Gestational age < 32 weeks	1.929	0.808	6.884	1.411 to 33.574	0.017
Respiratory support (ventilator and HFOV)	1.796	0.641	6.026	1.715 to 21.173	0.005
Male	1.041	0.659	2.832	0.779 to 10.297	0.114
Constant	-.664	0.957	0.009		0.000

Discussion

Of 116 subjects, most subjects experienced IVH grade 1 (75%). Similarly, Danni found that IVH grade 1 was more common than other IVH grades, with an incidence of 52.5%.[12] Previous studies also reported IVH grade 1 as the most frequent (40% and 48.39%, respectively). We had a larger percentage of subjects with IVH grade 1 since our subjects were of older gestational age than subjects of the other studies.[16,17]

The male to female ratio was 1.42:1, with an OR exceeding 1 in bivariate analysis, Hence, the difference was not statistically significant. Multivariate analysis also revealed that sex was not a statistically significant factor for severe IVH. Other studies also reported more males with IVH than females, but not significantly different.[18,19]

Most subjects (89.5%) with IVH grade >2 had gestational age <32 weeks; this result was statistically significant (OR 11.610; 95%CI 2.540 to 53.058; P=0.000). Multivariate analysis revealed that gestational age was also significantly associated with IVH grade >2 occurrence (OR 6.884). A study reported that gestational age and weight were risk factors for the occurrence of severe IVH.[20] Babies born at gestational age <32 weeks have subependimal areas consisting of dense vascular networks. The microvasculartur in this germinal matrix is fragile because it has blood vessels that exhibit paucity of pericytes and immature basal lamina. The germinal matrix is vulnerable to hemorrhage and has a poorly-supported, extravascular network that remains up to gestational age <35 weeks. In addition, the auto-regulation mechanism in preterm infants is not fully developed, resulting in younger babies being more susceptible to IVH.[17,21] Birth weight was

not significantly associated with IVH grade >2 in multivariate analysis. The differing results in birth weight and gestational age was likely due to the fact that gestational age is more accurate in reflecting immaturity than birth weight.[17]

We found no statistically significant differences between manual PPV and IVH severity. Duration of PPV in this study was quite varied, possibly affecting our results. In addition, the occurrence of severe IVH is determined by immaturity of the cerebrovascular system and the vulnerability of the germinal matrix.[1,21]

A previous study reported that vaginal delivery increases the risk of IVH.[17] Vaginal birth results in a condition of hypoperfusion-reperfusion.[17,21] In this study, the percentage of vaginal deliveries with IVH grade >2 was greater than with IVH grade ≤2, although not significantly different, similarly with Linder *et al*.[22] Vaginal delivery should not be indicated in preterm infants likely to have a birth weight ≤1,500 g. In subjects who were delivered vaginally, there was more IVH grade >2 in subjects with birth weight ≤1,500 grams, although the difference was not statistically significant (P = 0.402).

Another study reported that HFOV usage increased the incidence of severe IVH (OR 4.8; 95%CI 1.3 to 17.3).[20] The use of HFOV changes the pCO2 parameters, resulting in cerebral blood flow fluctuations. Transcutaneous pCO2 tools are needed to monitor this condition. In our study, the use of HFOV was found in only five (4.3%) subjects, four of whom (80%) experienced IVH grade >2. This number of subjects with HFOV was too small to assess for statistical significance. For analysis purposes, we combined subjects with HFOV and subjects who used ventilators (79% of IVH grade >2). Both bivariate and multivariate analyses revealed that the use of ventilators and HFOV had a significant relationship with the occurrence of IVH grade >2 (OR 6.03; 95%CI 1.72 to 21.17). A study also reported that the use and duration of mechanical ventilation was associated with severe IVH (OR 2.7).[23] The use of mechanical ventilation leads to increased central venous pressure, causing episodic occurrence of cerebral perfusion disturbances and increasing the risk of IVH.[17,21]

Most subjects (85.3%) with clinical sepsis had IVH, either proven or not proven through blood cultures. Sepsis influences the occurrence of IVH by blood pressure disorders that lead to the disruption of cerebral blood flow. Also, the fragility of blood vessels in the germinal matrix can be exacerbated by an inflammatory effect on the blood-brain barrier.[21] Linder *et al*. reported that sepsis increased the risk of IVH (OR=8.19).[22] However, in our bivariate analysis, we found no significant differences between the IVH grades ≤2 and >2 in the cases of sepsis. Hence, sepsis may affect the occurrence of IVH, but not necessarily the severity of IVH.

The role of coagulopathy in the pathogenesis of IVH is unclear. A study of mutations in coagulation proteins evaluated the possibility of genetics as a risk factor for the occurrence and severity of IVH.[24] Genetic variation in the vitamin K-dependent coagulation system affected coagulation profiles and the risk of IVH in premature infants.[25] In our study, only 48.3% of subjects had medical record data on PT and aPTT. We found no significant differences between the number of subjects with > 2x the normal values of PT or aPTT and the severity of IVH. These results indicate that coagulopathy may not play a major role in the occurrence of IVH, but it is difficult to assess since we had a limited number of subjects.

Cerebral autoregulation of cerebral blood vessels encompasses the ability to maintain the cerebral blood flow to keep it relatively constant despite the fluctuations in systemic blood pressure. Unfortunately, only 24 of our subjects had blood pressure data. Twenty-two of these subjects (91.7%) experienced fluctuations in blood pressure. Bivariate analysis revealed no significant differences between those with blood pressure variations vs. those who did not, in terms of IVH severity. Hypotension was diagnosed in 20-45% of premature infants.[26] A correlation between hypotension and IVH has been inconclusive.[21] Hypotension may result in a decrease in cerebral blood flow and can result in injury to the germinal matrix capillaries through reperfusion mechanisms.[27] In this study, hypotension was not a significant factor. In contrast, a previous study reported that mean blood pressure was lower in infants with IVH grade ≥2.[28] A study also reported that hypotension was an independent risk factor for the occurrence of IVH in premature babies, and hypotension was found more often in IVH grade 3 and 4.[27] This difference in results may be due to our small number of subjects with blood pressure data.

Intraventricular hemorrhage has been reported to occur mostly within the first week of life, with 50% occurring in the first day after birth, up to 90% by the third day, and almost 100% detected by the seventh day of cranial ultrasound examinations.[24] In our study, IVH occurred in only 31.9% of subjects in the first week, with 19.8% detected by the third day, and reaching 60% in the second week. The low incidence of IVH in the first week in our study population was due to the not performing cranial ultrasounds on schedule. The high incidence of IVH present after the first week shows that cranial ultrasound to detect the presence of IVH should be done serially in infants with a high risk of IVH (gestational age <32 weeks and those using respiratory suppport, such as ventilator and HFOV, despite previous normal cranial ultrasound findings).

Thrombocytopenia was reported to be a risk factor for IVH.[21] Thrombocytopenia appears to be an independent cause of IVH. But some studies have also shown that in preterm infants, prostacyclin levels increase before IVH occurs. Prostaglandins not only have an effect on platelet function, but also other factors such as cerebral blood flow and the production of free radicals. Hence, platelets as an independent factor for the occurrence of IVH remains unclear.[3] Bivariate analysis revealed that platelets count <100,000/uL was significantly associated with IVH grade > 2 (OR 3.4; 95%CI 1.23 to 9.31). The incidence of IVH grade >2 with platelets count <100,000 /uL was 28.2% compared to 10.4% with platelets ≥100,000/uL. These results are consistent with a prospective study by Kahn *et al*. on infants <1,500 g. They reported an incidence of 20.7% in IVH grade >2 with platelets <100,000/uL, compared to 6.4% without thrombocytopenia.[4] Bolat *et al*.[6] and Von Lindern *et al*.[1] also reported that IVH grade ≥2 was more common in neonates with thrombocytopenia than without. In contrast, a previous study reported that there was no significant correlation between thrombocytes and IVH.[5] Differences in results may be due to the statistical analysis being conducted at differing levels of platelets and/or IVH. As such, Baer *et al*. by matching the gestational age and weight, found that subjects with IVH grade >2 had a significantly lower number of platelets compared to subjects without IVH.[5]

Pathogenesis of IVH is multifactorial, therefore, multivariate analysis was done to determine the strength of the correlation between the thrombocytopenia and the severity of IVH. Factors that were significantly associated with severe IVH were gestational age <32 weeks and respiratory support (ventilators and HFOV). A thrombocyte count <100,000/uL was not a major risk factor for the occurrence of IVH grade > 2. Some of the factors that cause thrombocytopenia were found to be not significant in IVH grade > 2, as thrombocyte counts and cranial ultrasound were not always performed on the same day. Also, cranial ultrasound showed resolved results in some cases, so that the exact timing between the thrombocytes and IVH was difficult to assess. In addition, the research was done in subjects with various degrees of IVH, and not compared to subjects without IVH.

This study found no correlation (r=0.21) between the severity of thrombocytopenia and severity of IVH. The results are in line with two previous studies who found no significant correlation between the severity of thrombocytopenia and severity of IVH.[1,9] This result is likely due to the complexity of IVH in neonates, not only depending on platelets counts. Recent data showed that thrombocyte dysfunction and thrombocyte coagulation disorders may play an important role in the occurrence of IVH.[29] Currently, the combination of thrombocytopenia and thrombocyte dysfunction is known to be an important factor in the high incidence of IVH in premature infants. Studies on adhesion, aggregation, and activation of thrombocytes showed that thrombocyte hyporeactivity lasted until 3-4 days after birth in aterm or premature infants.[30] Other studies reported that thrombocyte hyporeactivity lasted longer, but generally functional improvement was observed after 10-14 days.[30,31] A study concluded that the time needed to repair thrombocyte hyporeactivity cannot be ascertained.[32] Gestational age and chronological age affect thrombocyte function. As such, thrombocytopenia has varying effects in neonates, in terms of primary hemostasis and risk of hemorrhage. In addition, other factors such as the fragility of the germinal matrix and hemodynamic instability also have important roles.[31] Moreover, the lower number of subjects with IVH grade > 2 compared to the IVH degree ≤2 might have affected the results of the analysis.

In conclusion, the characteristic our IVH study subjects are largely males, birth weight

<1,500 g, gestational age 32-34 weeks, born via Caesarean section, used ventilator respiratory support, experienced sepsis, and suffered from IVH grade 1. The factors that have potentially significant associations with IVH grade >2 from bivariate analysis are gestational age <32 weeks, birth weight ≤1,500 g, use of ventilator or HFOV, and platelets count <100,000/uL. The incidence of severe IVH with platelets <100,000/uL is 28.2% compared to 10.4% with platelets ≥100,000/uL. Multivariate analysis reveals that severe IVH is significantly associated with gestational age <32 weeks and the use of respiratory support in form of a ventilator or HFOV. The severity of thrombocytopenia is not correlated with the severity of IVH (correlation coefficient 0.21).

Suggestion

Routine cranial ultrasounds should be performed on premature infants with gestational age <32 weeks (with or without ventilator or HFOV assistance) to detect the presence of IVH. The examinations should be carried out at the first week of life and repeated as indicated by the results of previous ultrasound or clinical conditions, especially in patients using ventilators or HFOV and with thrombocytopenia (platelets count <100,000/uL). Health centers with perinatalogy services should have cranial ultrasound facilities and competent human resources. We recommend a further, prospective study in infants of gestational age <32 weeks, to undergo cranial ultrasound and thrombocytopenia screening with weekly retrials or according to clinical conditions, to monitor for IVH and the timing of thrombocytopenia. It would be helpful to assess the prophylactic administration of thrombocytes suspensions to prevent IVH.

Conflict of interest

None declared.

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