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Characteristics of hemodynamics in cerebral vessels in non-traumatic intracranial hemorrhages

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Aim – to characterize cerebral hemodynamic disturbances in newborns with intracranial non-traumatic hemorrhages (INTH) depending on the severity of the condition, in order to optimize treatment strategies for perinatal pathologies.
Materials and methods. The study was conducted at the Azerbaijan Republician Perinatal Center. Neurosonography was performed on 800 full-term newborns within the first 24 hours of life, and on 192 preterm newborns depending on their condition: 50 infants on day 1, 99 – on day 3, 27 – on day 5, and 20 – on day 7. Using this method, the maximal systolic velocity (Vmax), minimal diastolic velocity (Vmin), and resistance index (RI) were measured. Statistical analysis of the obtained results was performed in Excel: the mean values and standard errors were calculated.
Results. Ventricular dilatation was recorded in 6 infants. In preterm infants (gestational age ≤36 weeks) with and without INTH, the Vmax in the anterior cerebral artery was 0.27±0.005 and 0.30±0.006 m/s, the Vmin was 0.007±0.001 and 0.009±0.001 m/s, and the mean flow velocity was 0.18±0.005 and 0.20±0.004 m/s, respectively, demonstrating statistically significant differences between the groups. Hemodynamics were comparatively slower in infants with INTH. The Vmin in the anterior cerebral artery differed significantly between preterm and full-term infants without INTH (0.09±0.01 and 0.10±0.02 m/s), with lower values in preterm infants. A similar pattern was found when comparing preterm and full-term infants with INTH (0.07±0.001 and 0.08±0.002 m/s). The mean flow velocity in the anterior cerebral artery differed significantly between preterm infants with INTH (0.18±0.005 m/s) and without INTH (0.20±0.004 m/s). Comparable statistically significant differences were also observed between full-term infants with INTH (0.19±0.005 m/s) and without INTH (0.20±0.004 m/s).
Conclusion. In newborns with INTH, cerebral hemodynamics slow down proportionally to the severity of hemorrhage. The more severe the hemorrhage, the greater the hemodynamic delay. Therefore, large-scale neurosonographic screening of newborns in perinatal centers is essential.
The study complied with the principles of the Declaration of Helsinki and was approved by the institutional Ethics Committee. The informed consent was obtained from the patients prior to participation.
The author declares no conflict of interest.
Keywords: non-traumatic hemorrhages, intracranial, hemodynamics, cerebral vessels, newborn.

Характеристики гемодинаміки в судинах головного мозку при нетравматичних внутрішньочерепних ураженнях

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Мета – охарактеризувати порушення церебральної гемодинаміки в новонароджених із внутрішньочерепними нетравматичними крововиливами (ВЧНТК) залежно від тяжкості стану для оптимізації стратегій лікування перинатальних патологій.
Матеріали та методи. Дослідження проведено в Перинатальному центрі Азербайджанської Республіки. Нейросонографію проведено 800 доношеним новонародженим протягом перших 24 годин життя, 192 недоношеним новонародженим залежно від їхнього стану: 50 немовлят – на 1-й, 99 – на 3-й, 27 – на 5-й та 20 немовлят – на 7-й день. За допомогою цього методу виміряно максимальну систолічну швидкість (Vmax), мінімальну діастолічну швидкість (Vmin) та індекс резистентності (RI). Статистичний аналіз отриманих результатів проводився в Excel: розраховувалися середні значення та стандартні помилки.
Результати. Розширення шлуночків було зареєстровано у 6 немовлят. У недоношених дітей (гестаційний вік ≤36 тижнів) з ВЧНТК та без неї Vmax у передній мозковій артерії становила 0,27±0,005 та 0,30±0,006 м/с, Vmin – 0,007±0,001 та 0,009±0,001 м/с, а середня швидкість кровотоку – 0,18±0,005 та 0,20±0,004 м/с, відповідно, що демонструє статистично значущі відмінності між групами. Гемодинаміка була дещо повільнішою в дітей із ВЧНТК. Vmin у передній мозковій артерії суттєво відрізнялася в недоношених та доношених дітей без ВЧНТК (0,09±0,01 та 0,10±0,02 м/с), з нижчими значеннями в недоношених дітей. Подібну закономірність було виявлено під час порівняння недоношених та доношених дітей із ВЧНТК (0,07±0,001 та 0,08±0,002 м/с). Середня швидкість кровотоку в передній мозковій артерії суттєво відрізнялася між недоношеними дітьми з ВЧНТК (0,18±0,005 м/с) та без ВЧНТК (0,20±0,004 м/с). Порівняні статистично значущі відмінності спостерігалися між доношеними дітьми з ВЧНТК (0,19±0,005 м/с) та без ВЧНТК (0,20±0,004 м/с).
Висновок. У новонароджених із ВЧНТК церебральна гемодинаміка сповільнюється пропорційно тяжкості крововиливу. Чим сильніший крововилив, тим більша гемодинамічна затримка. Тому масштабне нейросонографічне обстеження новонароджених у перинатальних центрах є надзвичайно важливим.
Дослідження відповідало принципам Гельсінської декларації та було схвалено комітетом з етики установи. Інформовану згоду пацієнтів було отримано перед участю.
Автор заявляє про відсутність конфлікту інтересів.
Ключові слова: нетравматичні крововиливи, внутрішньочерепні, гемодинаміка, судини головного мозку, новонароджений.

Introduction

In recent years, the capabilities provided by radiation diagnostics have facilitated the diagnosis of non-traumatic intracranial hemorrhages (NTICH), leading scientists to begin researching this pathology more actively. The 10th and 11th Revisions of the International Classification of Diseases list 7 types of NTICH (KA92.0. Non-traumatic intraventricular hemorrhage Grade I; KA92.0. Non-traumatic intraventricular hemorrhage Grade I; KA92.1. Non-traumatic intraventricular hemorrhage Grade II; KA92.2. Non-traumatic intraventricular hemorrhage Grade III; KA92.3. Non-traumatic intraventricular hemorrhage Grade IV; KA92.4. Non-traumatic cerebral hemorrhage; KA92.5. Non-traumatic subarachnoid hemorrhage; KA92.6. Non-traumatic cerebral haemorrhage) were determined. Modern variants of radiation diagnostics allow for the precise determination of NTICH size, location, and areas of damage [2,6]. Hemodynamics of cerebral vessels in specific intracranial hemorrhages have been extensively presented in the literature [5,8,9]. Neurosonography has particularly enabled the detection of hemodynamic disturbances in prematurely born infants [1,3,7]. It is considered appropriate to perform dopplerography on all newborns with a gestational age of less than 32 weeks [10].

The aim of the study to characterize hemodynamic disturbances in cerebral vessels in the context of non-traumatic intracranial hemorrhages, and depending on their severity, for optimizing treatment tactics of prenatal pathologies.

Materials and methods of the study

The Azerbaijan Republician Perinatal Center was chosen as the observation site for the study. Our observation group included 996 live-born infants, which fully ensures the statistical significance of the expected epidemiological characteristics. The diagnosis of NTICH was confirmed in 156 newborns based on monitoring, neurological clinical examination, and instrumental assessment (neurosonography). Infants were divided into two groups: 750 in term (gestational age more than 36 completed weeks) – group Full-term and 246 premature (≤36 weeks gestational age) – group Preterm. Two subgroups were distinguished in each group: 156 newborns with (subgroup NTIH+) and 800 without NTIH (subgroup NTIH-).

Neurosonography was performed on all interm children (800) on the first day, and on the first (50), third (99), fifth (27), and seventh (20) days, depending on the condition of the premature infants (192). The maximum systolic velocity (Vmax), minimum diastolic velocity (Vmin), and resistance index (RI) were determined by this method. Resistance index (RI): = (Vmax – Vmin) / Vmax.

A number of indices were obtained using this method, among which the maximal systolic velocity (Vmax), minimal diastolic velocity (Vmin), and RI are of particular importance. A high RI (>0.70) indicates increased vascular resistance. A low RI (<0.55) is an indicator of decreased resistance and hyperemia. A normal RI (0.55–0.70) indicates normal perfusion and healthy vascular tone. These indices were determined in the anterior cerebral artery (ACA), internal carotid artery (ICA), and basilar artery (BA).

The statistical processing of our obtained results was performed in the Excel program [4]. Since the majority of the indices we used were qualitative features, their description was provided using criteria intended for these features (the number of NTICH cases per 100 children; the number of antenatal and intranatal features; the standard error of these indices; 95% confidence interval). $p<0.05$

Results of the study and discussion

Based on the following characteristics: one or two distinct subependymal hemorrhages at the level of the germinal matrix (>10 mm), the diagnosis of NTICH Grade I was determined. This diagnosis was detected in 61 infants, whose body weights were respectively <1000 g, 1000–1500 g, 1500–2000 g, 2000–2500 g, and ≥2500 g in the groups of 1, 6, 23, 21 and 10 infants.

The Grade II NTICH was diagnosed in 51 infants, in which the hemorrhage filled the ventricular cavity (>10 mm) without causing ventricular enlargement was detected. The body mass of 5, 12, 12, 12, and 10 of these infants was <1000 g, 1000–1500 g, 1500–2000 g, 2000–2500 g, and ≥2500 g.

The Grade III–IV NTICH was diagnosed in 27 children when the hemorrhage enlarged the ventricular size, when thrombus visualization was recorded, and when other associated signs were present. The body mass of 7, 9, 5, 3, and 3 of these children was <1000 g, 1000–1500 g, 1500–2000 g, 2000–2500 g, and ≥2500 g.

Hemorrhage in other regions (cerebral parenchyma, cerebellum, etc.) was recorded in 17 infants, body mass of 8, 3, 4, 0, and 2 of them was <1000 g, 1000–1500 g, 1500–2000 g, 2000–2500 g, and ≥2500 g.

Post-haemorrhagic hydrocephalus was recorded in 12 infants (among those with Grade III–IV NTICH). Hypoxic foci in the cerebral parenchyma were detected in 103 children. Neurosonography was performed in all full-term infants (800) on the first day, and in immature infants (192), it was carried out on the first (50 individuals), third (99), fifth

Table 1

Dopplerographic Indices of Cerebral Hemodynamic in newborns with and without NTICH (μ±m)

Vessels	Indicators	Preterm		Full-term	
		NTICH+	NTICH-	NTICH +	NTICH -
Anterior Cerebral Artery, m/s	Vmax	0.27±0.005*	0.30±0.006**	0.30±0.01*	0.33±0.02
	Vmin	0.07±0.001*	0.09±0.001**	0.08±0.002*	0.10±0.002
	V, average	0.18±0.005*	0.20±0.004	0.19±0.004*	0.21±0.005
	RI	0.68±0.008*	0.71±0.009**	0.70±0.007*	0.73±0.009
Internal Carotid Artery, m/s	Vmax	0.42±0.007*	0.46±0.006**	0.46±0.005*	0.50±0.007
	Vmin	0.11±0.002*	0.12±0.003	0.11±0.002*	0.13±0.002
	V, average	0.26±0.004*	0.29±0.005	0.28±0.005*	0.31±0.007
	RI	0.71±0.009*	0.74±0.009**	0.73±0.011*	0.76±0.010.
Basilar Artery, m/s	Vmax	0.40±0.005*	0.42±0.006**	0.42±0.006**	0.44±0.007
	Vmin	0.10±0.001*	0.11±0.001	0.11±0.002*	0.13±0.002
	V, average	0.26±0.006*	0.28±0.007	0.27±0.007*	0.29±0.008
	RI	0.72±0.011*	0.75±0.009**	0.74±0.010*	0.77±0.011

Notes: RI – Resistance Index; V – Velocity; Vmax – Maximal Systolic Velocity; Vmin – Minimal Diastolic Velocity; * – p<0.05 for comparison between groups with and without Non-traumatic Intracranial Hemorrhages (NTICH); ** – for comparison between the mature and immature groups.

(27), and seventh (20) days, depending on their condition. The ventricular dilatation was detected in 6 children.

Characteristics of cerebral hemodynamics in neonates with and without NTICH are presented in Table 1.

The maximal systolic velocity in the anterior cerebral artery was statistically significantly different between the groups, constituting 0.27±0.005 and 0.30±0.006 ($p<0.05$). Similarly, the minimal diastolic velocity was 0.007±0.001 and 0.009±0.001 ($p<0.005$), and the mean velocity was 0.18±0.005 and 0.20±0.004 m/s ($p<0.05$), all differing statistically significantly from each other in preterm newborns (⩽36 weeks gestation age) with and without NTICH. Hemodynamics are relatively slower in children with NTICH.

Maximal systolic velocity in the anterior cerebral artery (U_{max}) is 0.33±0.02 m/s (95% confidence interval 0.29–0.37m/s) in full-term healthy (without NTICH) infants (gestation age ⩾37 weeks). Corresponding indices in preterm infants (gestation age ⩽36 weeks) of the same category (NTICH+; NTICH-) were 0.30±0.006 m/s (95% confidence interval 0.29–0.31 m/s) and 0.27±0.005 m/s (95% confidence interval 0.26–0.28m/s). Paired comparison of these indicators showed that the maximal systolic blood flow velocity in the Anterior Cerebral Artery is different between preterm and term infants without Non-traumatic Intracranial Hemorrhages (NTICH) ($p<0.05$), and blood flow velocity is relatively lower in preterm infants. While comparing the maximal velocity in the anterior cerebral artery of preterm and full-term infants with and without NTICH, we obtain the same result. It approves that the maximal blood flow velocity in the anterior cerebral artery significantly differs ($p<0.05$) between preterm infants, irrespective of the presence or absence of NTICH.

The minimal diastolic blood flow velocity in the Anterior Cerebral Artery statistically significantly differs ($p<0.05$) between preterm and term infants without NTICH (0.09±0.01 m/s and 0.10±0.02 m/s, respectively), with the level of the index being lower in preterm infants. A similar result is observed in the comparison of preterm and term infants with NTICH (0.07±0.001 m/s and 0.08±0.002 m/s).

Comparing the minimal diastolic flow rate in the anterior cerebral artery also gives us reason to reject the null hypothesis in premature and full-term infants with and without NTICH.

The mean blood flow velocity in the anterior cerebral artery significantly differs in groups of premature infants with (0.18±0.005 m/s, 95% confidence interval 0.17–0.19 m/s) and without NTICH ($p<0.05$). The similar results were observed in full-term newborns with (0.19±0.004 m/s) and without (0.21±0.005 m/s) NTICH.

The RI of the anterior cerebral artery was 0.73±0.009 (95% confidence interval 0.2–0.75) in full-term newborns without NTICH (in practically healthy children). In the comparison with the other three groups (premature newborns with and without NTICH, full-term newborns with NTICH), the RI

Table 2

Dopplerographic indicators of cerebral hemodynamics in newborn with and without NTCH (μ±m)

Vessel	Indicators	Grade IV NTICH	Grade III NTICH	Grade II NTICH	Grade I NTICH ə
Anterior cerebral artery, m/s	Vmax	0.21±0.003*	0.26±0.004*	0.28±0.001*	0.30±0.002
	Vmin	0.05±0.001*	0.08±0.001*	0.09±0.002*	0.10±0.002
	Vaverage	0.13±0.004*	0.17±0.004*	0.19±0.004*	0.21±0.005
	RI	0.58±0.008*	0.62±0.009*	0.68±0.007*	0.71±0.009
Internal carotid artery, m/s	Vmax	0.38±0.005*	0.42±0.004*	0.46±0.005*	0.48±0.005
	Vmin	0.10±0.002*	0.12±0.003*	0.13±0.002*	0.14±0.002
	Vaverage	0.24±0.004*	0.28±0.005*	0.29±0.005*	0.31±0.007
	RI	0.61±0.009*	0.64±0.009*	0.70±0.011*	0.72±0.010.
Basilar artery, m/s	Vmax	0.35±0.005*	0.38±0.006*	0.40±0.006 *	0.42±0.007
	Vmin	0.09±0.001*	0.10±0.001*	0.11±0.002*	0.12±0.002
	Vaverage	0.22±0.006*	0.24±0.007*	0.26±0.007*	0.27±0.008
	RI	0.62±0.011*	0.65±0.009*	0.68±0.010*	0.71±0.011

Notes: RI – resistance index; V – velosity; Vmax – maximal systolic velocity; Vmin – minimal diastolic velocity; * – p<0.05.

of the anterior cerebral artery (respectively 0.68±0.008; 0.71±0.09 and 0.70±0.007) was statistically significantly lower (p<0.05). Thus, for patients with NTICH, relatively low levels of maximal systolic velocity, minimal diastolic velocity, and vascular resistance in the anterior cerebral artery are characteristic.

The maximal systolic velocity of blood in the internal carotid artery was lower than the corresponding indicator in the anterior cerebral artery. The indicator varied in the range of 0.42±0.007 m/s to 0.50±0.007 m/s, showing a significant difference between them. The relatively low-level indicator was recorded in the premature group with NTICH, while the relatively high-level indicator was recorded in the term-born group without NTICH. The maximal systolic velocity of blood in the internal carotid artery of children with and without NTICH differs significantly from each other, both in the premature (0.42±0.007 and 0.46±0.006; p<0.05) and full-term (0.46±0.005 m/s and 0.50±0.007 m/s) children. This data proves the decrease in the maximal systolic velocity of blood in the arteries against the background of NTICH.

The minimal diastolic velocity of blood in the internal carotid artery didn't differ in premature and full-term infants with NTICH (0.11±0.002 m/s and 0.11±0.002 m/s), but in infants without NTICH (0.12±0.003 m/s and 0.13±0.002 m/s) was statistically significantly lower. In the compared groups, the statistically significant difference is greater than the mean blood flow velocity in the internal carotid artery. Indicators were lower in newborns with NTICH (0.26±0.004 and 0.28±0.005 m/s), and relatively high in newborns without NTICH (0.29±0.005 and 0.31±0.007 m/s). Thus, it was approved that the minimal, maximal, and moderate diastolic velocity of blood in the internal carotid artery is lower in newborns with NTICH.

All four groups in which we compared the RI of the internal carotid artery differed significantly from each other. The level of the indicator was 0.71±0.009 and 0.7±0.009 in premature children with and without NTICH, 0.73±0.011 and 0.76±0.010 in full-term infants. A decrease in resistance was also observed in these vessels against the background of NTICH.

A similar result due to hemodynamic velocity is also observed in the internal carotid artery and the basilar artery. In these vessels as well, both the maximal systolic and minimal diastolic velocities were relatively low in children with NTICH. The difference between the compared groups is more clearly visible based on the RI in all vessels. The RI in premature children with and without NTICH was 0.68±0.08 and 0.71±0.09 in the anterior cerebral artery, 0.71±0.09 and 0.74±0.04 in the internal carotid artery, and 0.72±0.11 and 0.75±0.09 in the basilar artery (p<0.05).

Thus, in premature newborns with NTICH, cerebral hemodynamics are relatively weak. The hemodynamic indicators in the cerebral vessels differ significantly between premature and full-term newborns with NTICH (p<0.05). Hemodynamics are relatively faster in full-term newborns with NTICH.

Comparing the cerebral hemodynamic indicators in full-term newborns with and without NTICH, a statistically significant difference is revealed. Against the background of NTICH, both the systolic and diastolic velocities, as well as the RI, are at a lower level in the cerebral vessels.

Thus, the hemodynamics of cerebral vessels change depending on both NTICH and on whether the child was term or preterm at birth.

The characteristics of hemodynamics in the cerebral vessels depending on clinical forms of NTICH are given in Table 2.

As can be seen, the maximal systolic velocity in the anterior cerebral artery varied in the range of 0.21 ±0.003 – 0.30 ±0.02 m/s, depending on the severity of NTICH. In the severe form of hemorrhage (Grade IV), the level of the indicator is statistically significantly lower, while in mild hemorrhages (Grade I), the indicator is considerably higher ($p<0.05$). A proportional difference is observed among the degrees of severity of the hemorrhage: the indicator decreases as the hemorrhage becomes more severe.

The minimal diastolic velocity of blood in the anterior cerebral artery was 0.05±0.01 m/s in infants with Grade IV NTICH, in infants with Grade III NTICH was significantly higher (0.08±0.001 m/s), and the proportional increasing trend continues as the severity of the pathology decreases: in Grade II NTICH, 0.09±0.002 m/s, 0.10±0.002 m/s in Grade I NTICH.

The mean blood flow velocity in the anterior cerebral artery also changed depending on the severity of NTICH; the relationship between the mean velocity and the severity of the hemorrhage is inversely proportional.

The vascular RI in the anterior cerebral artery was 0.71±0.009 in Grade I NTICH, 0.68±0.007 in Grade II NTICH, 0.62±0.009 in Grade III NTICH, and 0.58±0.008 in Grade IV NTICH. The difference in the indicators is statistically significant ($p<0.05$). The severity of the hemorrhage is inversely proportional to the vascular resistance.

The maximal systolic blood velocity in the internal carotid artery in Grade I–IV NTICH changes within a large interval; the lower velocity is observed in grade IV (0.38±0.005 m/s), and the higher velocity is observed in Grade I (0.48±0.005 m/s). In this vessel as well, the maximal systolic velocity changed inversely with the severity of the intracranial hemorrhage; the blood flow velocity tends to decrease as the pathology becomes more severe.

The minimal diastolic velocity in the internal carotid artery in the groups we observed (Grade I–IV NTICH) was 0.14±0.002 m/s, 0.13±0.003 m/s, and 0.10±0.002 m/s, respectively. These values differed significantly from each other ($p<0.05$), and the severity of the disease was inversely proportional to the blood flow velocity. A similar result was also observed for the mean blood flow velocity in the internal carotid artery: 0.27±0.008 m/s, 0.26±0.007 m/s, 0.24±0.007 m/s, and 0.22±0.006 m/s in Grade I–IV NTICH. In this vessel as well, the RI changed inversely with the severity of the hemorrhage: 0.61±0.009; 0.64±0.009, 0.70±0.011, and 0.72±0.010 in Grade IV-I NTICH, respectively.

The minimal diastolic velocity of blood in the basilar artery was 0.12±0.002 m/s in Grade I NTICH, 0.11±0.002 m/s in Grade II NTICH, 0.10±0.001 m/s in Grade III NTICH, and 0.09±0.001 m/s in Grade IV NTICH. These values differed significantly from each other ($p<0.05$).

The blood velocity in the basilar artery was respectively 0.27±0.008 m/s, 0.26±0.007 m/s, 0.24±0.007 m/s and 0.22±0.006 m/s in Grade I–IV NTICH. The RI of vessels in the basilar artery in this group of patients was inversely proportional to the severity of the disease: in Grade I–IV NTICH – 0.71±0.011, 0.68±0.010. 0.65±0.009 and 0.62±0.011.

Thus, blood flow velocity and vascular resistance in the cerebral arteries can be used as predictors of the severity degree of NTICH.

The general conclusion observed in the literature regarding the hemodynamics of children with central nervous system damage is that, in most cases, blood circulation in the cerebral vessels is weakened [5,8,9]. This fact is confirmed in our study: a decrease in both the maximal and minimal diastolic velocities in the anterior cerebral, internal carotid, and basilar arteries was proven in newborns with the diagnosis of intracranial non-traumatic hemorrhage compared to the control group (newborns without intracranial non-traumatic hemorrhage). Furthermore, we have shown that the blood flow velocity in the cerebral vessels changes inversely proportionally to the severity of the NTICH. Based on the obtained results, it can be noted that neurosonography allows to plan the prognosis of NTICH.

Conclusion

In infants born with diagnosed NTICH, the hemodynamics of the cerebral vessels slow down depending on the severity of the hemorrhage: hemodynamics are inversely proportional to severity degree: the impairment of hemodynamics increases as the degree of severity increases. That is why the mass neurosonographic examination of newborns in a prenatal center is important.

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