Russian Journal of Anaesthesiology and Reanimatology
2023, No. 5, pp. 32–39
https://doi.org/10.17116/anaesthesiology202305132

Cerebral perfusion in children with severe infections of the central nervous system

© K.YU. ERMOLENKO[1, 2], K.V. PSHENISNOV[2], YU.S. ALEKSANDROVICH[2], YU.P. VASILIEVA[1]

[1]Children's Research Clinical Center for Infectious Diseases, St. Petersburg, Russia;
[2]St. Petersburg State Pediatric Medical University, St. Petersburg, Russia

ABSTRACT

Background. Adequate cerebral perfusion is a major challenge in ICU children with severe infections of the central nervous system (CNS).

Objective. To establish the optimal indicators of systemic and cerebral perfusion in children with CNS infections and catecholamine support.

Material and methods. There were 100 children aged 3.5±2.6 years with severe CNS infections. GCS score at admission was 8.8±2.4 points. To assess the effectiveness of cerebral perfusion, we measured optic nerve diameter and performed transcranial Doppler neurosonography with calculation of resistance index in the middle cerebral artery. Oxygen saturation in brain parenchyma was assessed in 30 patients by using of cerebral oximetry. We measured transverse dimensions of hemispheres and lateral ventricles in all patients. All examinations were conducted in 1, 3 and 5 days after admission to ICU.

Results. The only significant indicator was resistance index in the middle cerebral artery. This value was significantly higher in deceased patients (0.65±0.11 vs 0.48±0.16; $p<0.05$). A correlation between optic disc diameter and GCS score was revealed ($R=0.52$; $p<0.005$). Severity of cardiovascular dysfunction correlated with resistance index in the middle cerebral artery ($R=0.61$; $p<0.005$). Optic disc diameter was not associated with outcomes of disease. Optimal cerebral perfusion is observed in patients with mean blood pressure 55—75 mm Hg.

Conclusion. Mean blood pressure should be maintained within 55—75 mm Hg in children with severe CNS infections requiring hemodynamic support.

Keywords: *CNS infections, children, intracranial hypertension, cerebral perfusion.*

INFORMATION ABOUT THE AUTHORS:
Ermolenko K.Yu. — https://orcid.org/0000-0003-1628-1698
Pshenisnov K.V. — https://orcid.org/0000-0003-1113-5296
Aleksandrovich Yu.S. — https://orcid.org/0000-0002-2131-4813
Vasilieva Yu.P. — https://orcid.org/0000-0002-4732-8623
Corresponding author: Pshenisnov K.V. — e-mail: psh_k@mail.ru

TO CITE THIS ARTICLE:
Ermolenko KYu, Pshenisnov KV, Aleksandrovich YuS, Vasilieva YuP. Cerebral perfusion in children with severe infections of the central nervous system. *Russian Journal of Anaesthesiology and Reanimatology = Anesteziologiya i Reanimatologiya*. 2023;5:32–39. (In Russ., In Engl.).
https://doi.org/10.17116/anaesthesiology202305132

Acute cerebral insufficiency is the main clinical sign of infections of the central nervous system in children. Severity of cerebral insufficiency affects the course of disease, outcomes and quality of life in long-term period [1].

Intracranial hypertension (ICH) is essential in pathogenesis of acute cerebral insufficiency. Therefore, correction of intracranial hypertension with prevention of cerebral edema and brain dislocation is important in intensive care. Optimal systemic arterial pressure and cerebral perfusion pressure maintain adequate cerebral blood flow and brain metabolism [2—4].

In routine clinical practice, the diagnosis of ICH is based on clinical data with subsequent neuroimaging. This approach is not always possible in critically ill patients, since we cannot make a timely and informed decision on the need for drug therapy for ICH and evaluation of its effectiveness in this case [5].

Ultrasound is also widely used to assess intracranial hypertension and cerebral edema in children with severe CNS infections. This method is available at the patient's bed in real time. Measuring the diameter of the optic nerve with membranes and transcranial Doppler neurosonography allow you to evaluate ICP in dynamics and under anti-edematous therapy, as well as to estimate its effectiveness [6]. Cerebrovascular resistance is one of the parameters characterizing efficiency of cerebral blood flow and ICH severity [7—9].

Obviously, persistent increase in ICP up to 15—20 mm Hg is accompanied by severe disturbances in cerebral blood flow autoregulation with reduced reserve of dilation of cerebral vessels. Therefore, there is a hypothesis that increased cerebrovascular resistance is a "harbinger" of cerebral vasospasm and ischemia [10—15].

Most studies devoted to cerebral perfusion indicate the need for constant ICP monitoring. Some authors emphasize better outcomes if adequate cerebral perfusion is a priority of therapy instead of decongestant therapy with diuretics [16—21].

However, studies devoted to this problem in adults and children are few, and some of them were carried out more than fifteen years ago. These facts inspired this research [21—25].

The purpose of the study was to establish the optimal indicators of systemic and cerebral perfusion in children with CNS infections and catecholamine support.

Material and methods

A retrospective observational single-center study included 100 ICU children aged 1 month — 18 years between 2016 and 2019.

The local ethics committee of the St. Petersburg State Pediatric Medical University approved this study (protocol No. 19/01 dated 12/17/22).

Inclusion criteria: a) severe CNS infections, b) > 2 signs of systemic inflammatory response and multiple organ failure; c) invasive mechanical ventilation. The diagnosis of systemic inflammatory response was based on international consensus criteria for sepsis in children [26].

Exclusion criteria: patients with organic diseases of the central nervous system, congenital and genetic diseases.

Mean age of patients was 3.5 ± 2.6 years. Boys prevailed (66% vs 34%). Most often, children with CNS infections were diagnosed with bacterial purulent meningitis (65%). The main causative agents of meningitis were meningococcus (42%), pneumococcus (8%) and Haemophilus influenzae (7%). Encephalitis occurred in 25% of patients. Unspecified bacterial and viral meningoencephalitis was found in 10% of cases. Mean GCS score was 8.8 ± 2.4 points at admission in the entire sample of patients (8.9 ± 2.26 and 6.4 ± 3.53 in survivors and deceased patients, respectively). Fifty-eight (58%) children required continuous infusion of inotropic and vasopressor drugs. We used catecholamine index to assess invasiveness of hemodynamic support [27]:

$$\textit{Catecholamine index} = \textit{dopamine, μg/kg/min} + \textit{dobutamine, μg/kg/min} + \textit{adrenaline, μg/kg/min} \times 100 + \textit{norepinephrine, μg/kg/min} \times 100$$

This value was 5 (0—25) in the entire sample (5 (0—24) in survivors and 112.5 (71.25—115.00) in dead patients). Septic shock was diagnosed in 44 (44%) patients upon admission to the ICU. Mean ICU-stay was 9.5 ± 6.2 days, duration of mechanical ventilation — 6.0 ± 3.9 days. Mortality rate was 10%. The main cause of mortality was progression of septic shock with circulatory failure.

According to the Pediatric Cerebral Performance Category Scale, 54 (60%) recovered patients had moderate neurological disorders at discharge from the ICU, 27 (30%) ones had trivial neurological impairment and 9 (10%) patients had severe central nervous system dysfunction.

In accordance with national and international recommendations, intensive care implied prevention and correction of ICH:

— invasive ventilation to maintain normal blood carbon dioxide pressure;
— sedation (benzodiazepines, barbiturate coma);
— maintaining mean blood pressure at the upper age-adjusted limit: 42% of patients received only volemic support, 58% of patients required constant infusion of inotropic and vasopressor drugs [28];
— maintaining serum sodium at the upper normal limit (at least 135—140 mmol/l);
— fluid balance control (ratio of diuresis to injected volume is not less than 70—80%);
— osmotic diuretics (mannitol 0.5 g/kg followed by 0.25 g/kg every 6 hours);
— anticonvulsant therapy according to indications.

We measured the diameter of the optic nerve with membranes in all patients. All ones underwent transcranial Doppler neurosonography upon admission and after 3 days. Ultrasound was performed using a linear and convex transducer (Mindray M7 scanner, Mindray™, China). We used resistance index in the middle cerebral artery to assess the effectiveness of hemodynamic support and severity of vasospasm. Cerebral oximetry was applied in 30 patients. In all patients, we measured transverse dimensions of hemispheres and lateral ventricles in 1, 3 and 5 days after admission to the ICU.

Statistical analysis was carried out using the Statistica for Windows v. 10 software package,(StatSoft, USA). Study power was estimated using t-test for independent samples. This value was 0.91 that indicated sufficient sample size [29]. Distribution normality was tested by using of Kolmogorov-Smirnov and Shapiro-Wilk tests. In case of normal distribution, data are presented as mean (Me) and standard deviation (SD). Abnormal distribution required median and percentiles. The hypothesis of statistical homogeneity of two samples was tested using Student's and Pearson's $\chi 2$ tests. Spearman correlation coefficient was used to analyze the relationship between variables [30].

Results

Cerebral perfusion parameters depending on outcomes of disease are presented in **Table 1**. There were no significant between-group differences in most cases. Only resistance index in the middle cerebral artery was significantly higher in deceased patients ($p<0.05$) **(Fig. 1)**.

There was a moderate negative correlation between optic disc diameter and GCS score (R=0.52; $p<0.005$) despite no significant between-group differences in isolated analysis of optic nerve diameter depending on the outcomes.

Transverse dimensions of hemispheres decreased and lateral ventricles enlarged after 5 days in all patients. Significant differences compared to baseline data were observed by the third day. Transverse dimensions of hemispheres decreased due to regression of brain edema, while lateral ventricles enlarged with the most noticeable changes within 3 days **(Table 2)**.

There were no significant differences in dimensions of hemispheres and lateral ventricles depending on the outcomes **(Fig. 2)**.

We found a strong positive correlation between severity of sepsis-related cardiovascular dysfunction and resistance index in the middle cerebral artery (R = 0.61; $p<0.005$) **(Fig. 3)**.

Table 1. **Cerebral perfusion parameters depending on outcomes of disease**

Variable	Recovery	Death	*p*-value
Optic disc diameter	6.01±0.74	5.93±0.4	>0.05
Cerebral oximetry	81.6±7.59	82.42 ±3.23	>0.05
Transverse dimension of hemispheres	67.21±6.05	67.21± 3.22	>0.05
Transverse dimension of ventricles	15.75±2.39	15.84±2.45	>0.05
Blood flow velocity in the middle cerebral artery	147.5±36.92	165.9±20.92	=0.05
Resistance index	0.48±0.16	0.65±0.11	<0.05

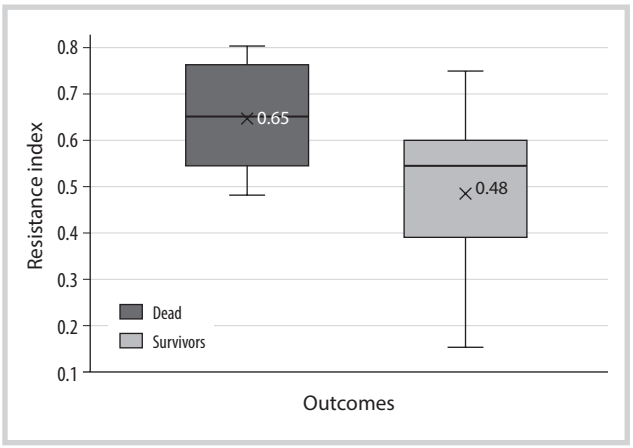


Fig. 1. **Resistance index depending on outcomes of disease.**

This indicates a high diagnostic value of resistance index. We can use this parameter as an indirect sign of reduced cerebral perfusion and progression of intracranial hypertension under vasospasm. A similar relationship was typical for mean blood pressure ($R = 0.81$; $p<0.005$) **(Fig. 4)**.

Systemic hemodynamics also affects severity of vasospasm. Therefore, one of the objectives was analysis of optimal mean blood pressure in patients requiring hemodynamic support to improve cerebral perfusion and eliminate intracranial hypertension. Mean blood pressure was 77.00 ± 4.65 mm in patients with resistance index > 0.6.

To determine the optimal mean blood pressure, we divided all patients requiring hemodynamic support into 2 groups. Group I included children with cerebral oxygenation increase by less than 10% within 2 days, group II — more than 10% (sign of effective intensive care).

Mean blood pressure 55—75 mm is accompanied by more significant increase of cerebral oxygenation **(Fig. 5)**. Therefore, these target values are advisable during infusion of sympathomimetics.

Discussion

Correction of intracranial hypertension and optimization of cerebral blood flow are ones of the most difficult objectives of intensive care in children with severe traumatic brain injury and severe infections of the central nervous system.

Currently, there are enough studies in international databases devoted to this problem. The authors emphasize invasive measurement of intracranial pressure as the "gold" standard for monitoring in this situation. However, this approach is possible only in a multi-field surgical hospital and has certain contraindications. In this regard, non-invasive measurement of ICP is of particular relevance, especially in children [31].

Despite numerous advantages, the majority of non-invasive methods for ICP measurement is less accurate and determines severity of ICH only in combination with clinical and diagnostic parameters. This is especially important in pediatric practice due to some functional features in these patients [32, 33].

One of the limitations of non-invasive techniques is operator-dependence. However, this shortcoming may be excluded if ICP is assessed in real time at the patient's bedside by one specialist [34].

Cerebral blood flow velocity is often assessed during neurosonography. However, this indicator was not associated with intracranial pressure and outcomes of disease in our study. Therefore, CBF should not be considered as a criterion of effective therapy [35].

At the same time, resistance index was the only indicator of cerebral blood flow correlating with severity of disorders

Table 2. **Dimensions of cerebral hemispheres and lateral ventricles**

Variable	Day 1	Day 3	Day 5
Transverse dimension of the right hemisphere, mm	65.13 ± 7.37	64.43 ± 4.20[a]	63.00 ± 8.17
Transverse dimension of the left hemisphere, mm	66.06 ± 4.29	63.82 ±7.93[a]	63.94 ± 3.67
Transverse dimension of the right lateral ventricle, mm	15.69± 2.35	17.23 ± 2.50[a]	17.38± 2.42
Transverse dimension of the left lateral ventricle, mm	15.97± 2.44	17.48± 2.90[a]	17.81± 2.71

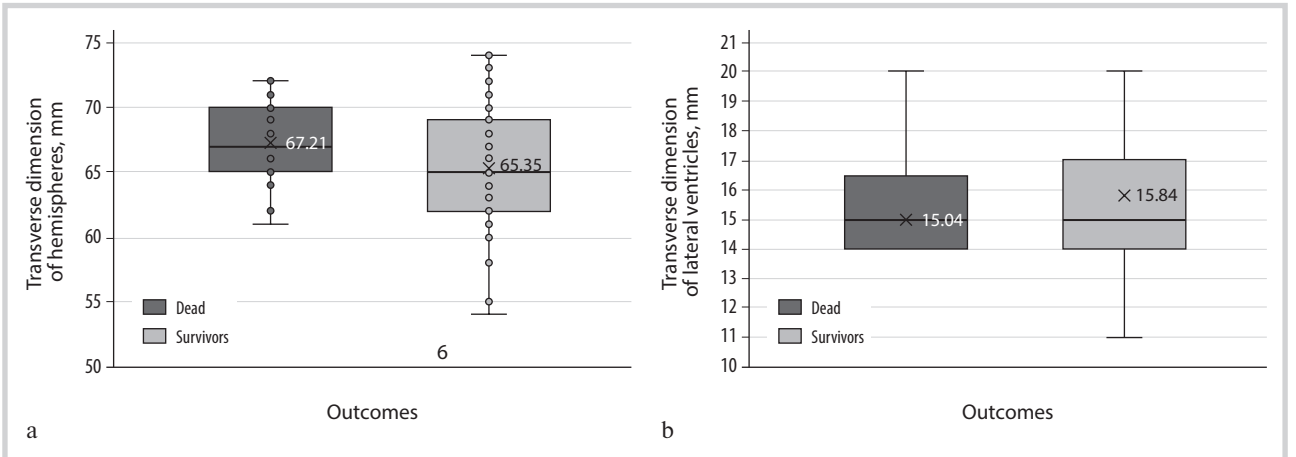


Fig. 2. **Dimensions of cerebral hemispheres and lateral ventricles depending on outcomes of disease.**

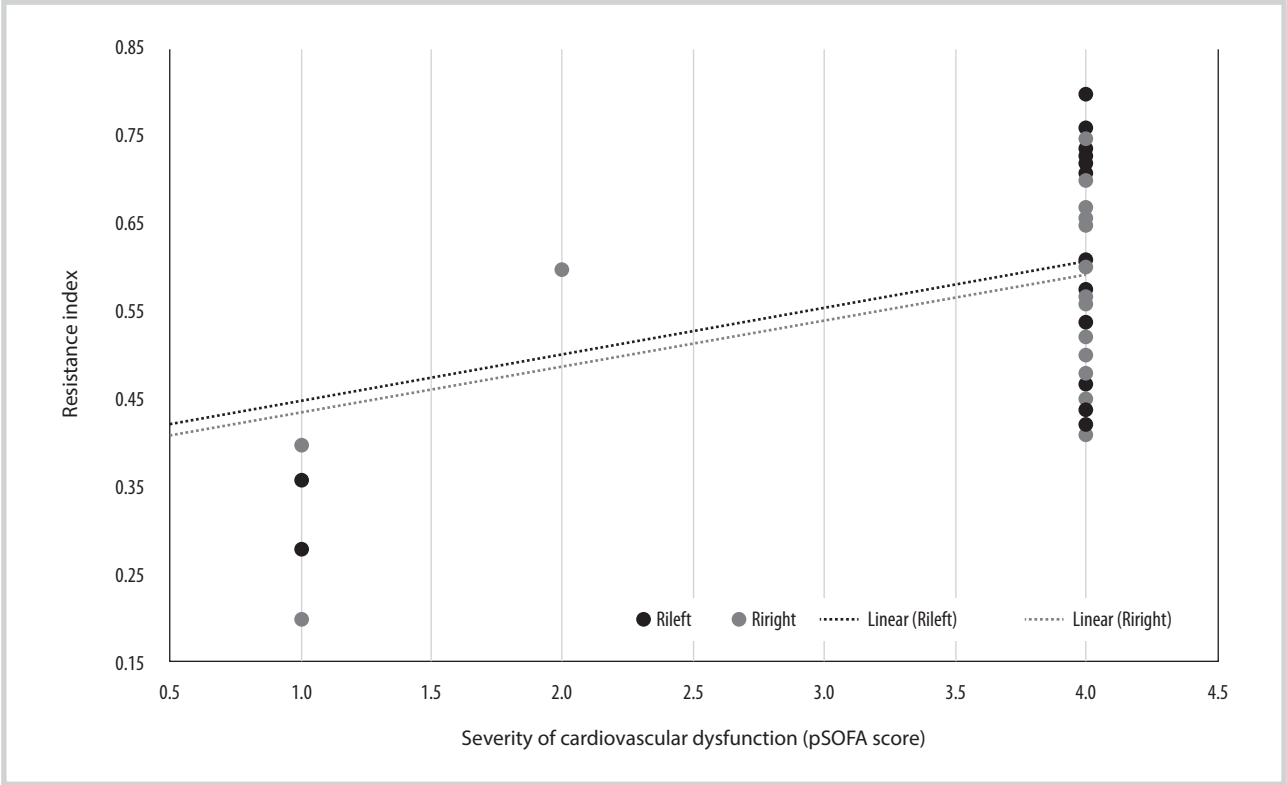


Fig. 3. **Correlation between severity of cardiovascular dysfunction (pSOFA scale) and resistance index in the middle cerebral artery.**

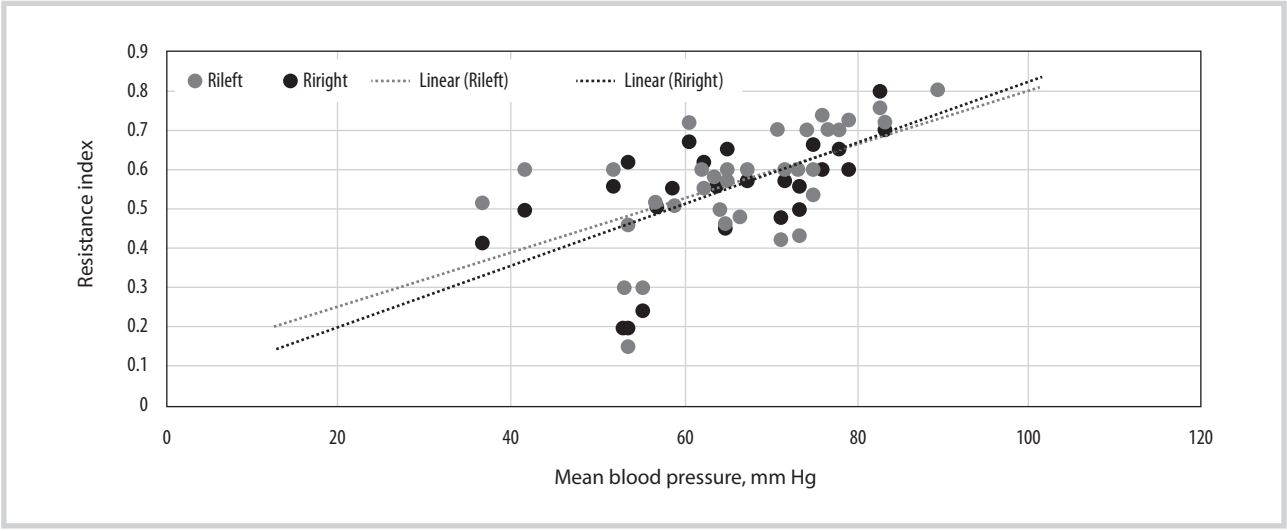


Fig. 4. **Correlation between resistance index in the middle cerebral artery and mean arterial pressure.**

and need for hemodynamic support to optimize cerebral perfusion pressure. Other authors reported similar data. Vasilyeva Yu.P. et al. [6] believe that vasospasm is critical in resistance index > 0.8.

We found no available studies devoted to assessment of intracranial hypertension based on neurosonography data. According to our study, dimensions of brain hemispheres and lateral ventricles within 3 days after admission to ICU are essential. Perhaps, this finding is due to complex therapy aimed at correction of intracranial hypertension (including osmotic diuretics) performed throughout this period. Risk of unfavorable outcomes is extremely high in case of ineffective 3-day intensive care and no positive ultrasonic changes.

Importantly, optic disc diameter did not significantly differ in both groups. Thus, we cannot use this parameter as a marker of ICH severity and predictor of unfavorable outcomes. Most likely, optic disc lesions occur only at the late stages of disease, when fatal outcome is expectable. We could not detect significant abnormalities of the optic nerve within 3-day intensive care and appropriate measurements in our patients [2].

Optimal mean blood pressure for adequate cerebral perfusion is one of the most controversial issues.

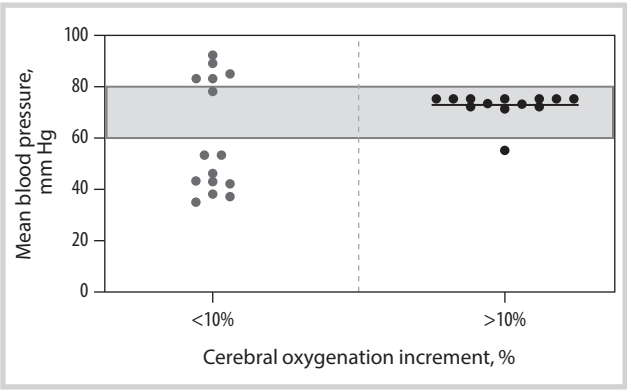


Fig. 5. **Optimal mean arterial pressure according to cerebral oximetry in patients with intracranial hypertension.**

Grande P.O. et al. [36] believe that excessive cerebral perfusion pressure can be not only unreasonable, but also dangerous (Lund concept). According to their opinion, it is necessary not only to increase perfusion pressure, but to achieve target indicators not exceeding 60 mm Hg. They consider arterial hypertension as a triggering factor for vasogenic cerebral edema due to phenomenon of "luxury perfusion" and excessive hydrostatic pressure in cerebral vessels. These data are consistent with the guidelines of the European Association for Pediatric and Neonatal Intensive Care. According to these recommendations, target mean blood pressure should be 65 mm Hg in children over 12 years old with the exception of patients with baseline arterial hypertension. Blood pressure is not the only target parameter in the treatment of patients with unstable hemodynamics. This is especially true for patients with acute cerebral insufficiency [37].

In routine clinical practice, the opinion of Rosner M.J. et al. [38] became more popular. The authors consider the minimum allowable cerebral perfusion pressure to be about 70 mm Hg in adults and do not establish the upper limit of systemic blood pressure. This approach is based on the hypothesis of "vasoconstrictor cascade". Increased systemic blood pressure activates autoregulation mechanisms, but these mechanisms do not function in full in patients with intracranial hypertension [10, 18].

Israilova V.K. et al. [20] demonstrated that cerebral oximetry is valuable for detection of cerebral blood flow disorders following progression of cerebral edema and timely correction of therapy for adequate cerebral perfusion. We confirm these data in our study. Higher cerebral oxygenation was typical at mean blood pressure 55—75 mm Hg. At the same time, cerebral oxygenation parameters did not significantly differ depending on the outcomes. Thus, we need to compare these parameters with other clinical and laboratory data under ongoing therapy.

Vasospasm is one of the main causes of deterioration in cerebral blood flow. Perhaps, aggressive hemodynamic support with high doses of catecholamines adversely affects the outcomes of disease. Therefore, intensive care in children with acute cerebral insufficiency should be aimed not only at preventing systemic hypoperfusion, but also cerebral vasospasm [18, 39]. Mean blood pressure is one of the few parameters that can be monitored in critically ill patients. Thus, there is an urgent need for further multiple-center studies to find target blood pressure in children with intracranial hypertension.

Conclusion

1. Resistance index of the middle cerebral artery is the most valuable parameter of cerebral blood flow in children with severe infections of the central nervous system.
2. Measurement of dimensions of brain hemispheres and lateral ventricles for assessing the effectiveness of intensive care is appropriate within 3 days after admission.
3. Optic disc dimension does not correlate with outcomes of severe infections of the central nervous system in children. However, this parameter may be used to assess severity of intracranial hypertension over time.
4. Mean blood pressure should be maintained within 55—75 mm Hg in children with severe CNS infections requiring hemodynamic support.

The study was not sponsored.
No conflict of interests to declare.

REFERENCES

1. Pshenisnov KV, Aleksandrovich YuS. Epidemiology of critical conditions in children of the metropolis. *Anesteziologiya i Reanimatologiya*. 2017;62(6):463-467. (In Russ.).
2. Aleksandrovich YuS, Pshenisnov KV, Gordeev VI. *Intensivnaya terapiya kriticheskikh sostoyanij u detej*. SPb: Izd-vo N-L; 2014. (In Russ.).
3. Pshenisnov KV. Hemodynamic support in children with severe traumatic lesions of the central nervous system. *Meditsina: teoriya i praktika*. 2018;3(4):160-164. (In Russ.).
4. Atiskov YuA, Akshulakov SK, Belkin AA, Kondratiev AN, Larionov SN, Nazaralieva ET, Riznich VP, Savvina IA, Safin ISh, Khachatryan VA. Craniospinal compliance — new principles for intracranial pressure monitoring. *Anesteziologiya i Reanimatologiya*. 2020;(6):37-43. (In Russ.). https://doi.org/10.17116/anaesthesiology202006137
5. Komantsev VN, Skripchenko NV, Voitenkov VB, Savina MV, Ivanova GP. Evoked potentials of the brain in neuroinfections in children. *Zhurnal infektologii*. 2013;5(2):55-62. (In Russ.).
6. Patent RF na izobretenie №2755648/17.09.21 Byull. №26. Vasilieva YuP, Klimkin AV, Skripchenko NV, Ostapenko BV. *Sposob diagnostiki stadii vnutricherepnoj gipertenzii pri nejroinfektsiyakh u detej v ostrom periode*. (In Russ.). Accessed July 28, 2023. https://patents.google.com/patent/RU2755648C1/ru
7. Dewey R, Pierer H, Hunt W. Experimental cerebral hemodynamics. Vasomotor tone, critical closing pressure, and vascular bed resistance. *Journal of Neurosurgery*. 1974;41(5):597-606. https://doi.org/10.3171/jns.1974.41.5.0597
8. Kasprowicz M. [*Assessment of cerebral hemodynamics based on pulse waveform analysis of intracranial pressure, arterial blood pressure and cerebral blood flow*]. Wrocław: Oficyna Wydawnicza Politechniki Wrocławskiej; 2012.
9. Kasprowicz M, Diedler J, Reinhard M, Carrera E, Steiner LA, Smielewski P, Budohoski KP, Haubrich C, Pickard JD, Czosnyka M. Time constant of the cerebral arterial bed in normal subjects. *Ultrasound in Medicine and Biology*. 2012;38(7):1129-1137. https://doi.org/10.1016/j.ultrasmedbio.2012.02.014
10. Rosin YuA. Cerebral hemodynamics in intracranial hypertension in children with bacterial purulent meningitis. *Pediatr*. 2011;2(3):32-34. (In Russ.).
11. Westermaier T, Pham M, Stetter C, Willner N, Solymosi L, Ernestus RI, Vince GH, Kunze E. Value of transcranial Doppler, perfusion-CT and neurological evaluation to forecast secondary ischemia after aneurysmal SAH. *Neurocritical Care*. 2014;20(3):406-412. https://doi.org/10.1007/s12028-013-9896-0
12. Sharples PM, Matthews DS, Eyre JA. Cerebral blood flow and metabolism in children with severe head injuries. Part 2: cerebrovascular resistance

and its determinants. *Journal of Neurology, Neurosurgery, and Psychiatry*. 1995;58(2):153-159. https://doi.org/10.1136/jnnp.58.2.153

13. Pluta RM. Delayed cerebral vasospasm and nitric oxide: review, new hypothesis, and proposed treatment. *Pharmacology and Therapeutics*. 2005;105(1):23-56. https://doi.org/10.1016/j.pharmthera.2004.10.002
14. Siemkowicz E. Cerebrovascular resistance in ischemia. *Pflugers Archiv*. 1980;388(3):243-247. https://doi.org/10.1007/BF00658489
15. Bhogal P, Yeo LL, Müller LO, Blanco PJ. The effects of cerebral vasospasm on cerebral blood flow and the effects of induced hypertension: a mathematical modelling study. *Interventional Neurology*. 2020;8(2-6):152-163. https://doi.org/10.1159/000496616
16. Ostapenko BV, Voitenkov VB, Marchenko NV, Skripchenko NV, Vasilieva YuP, Klimkin AV, Bedova MA. Modern techniques for intracranial pressure monitoring. *Meditsina ekstremal'nykh situatsij*. 2019;21(4):472-485. (In Russ.).
17. Tasker RC. Raised intracranial pressure during CNS infection: what should we do about it? *Critical Care Medicine*. 2014;42(8):1936-1938. https://doi.org/10.1097/CCM.0000000000000419
18. Kumar R, Singhi S, Singhi P, Jayashree M, Bansal A, Bhatti A. Randomized controlled trial comparing cerebral perfusion pressure-targeted therapy versus intracranial pressure-targeted therapy for raised intracranial pressure due to acute CNS infections in children. *Critical Care Medicine*. 2014;42(8):1775-1787. https://doi.org/10.1097/CCM.0000000000000298
19. Shetty R, Singhi S, Singhi P, Jayashree M. Cerebral perfusion pressure — targeted approach in children with central nervous system infections and raised intracranial pressure: is it feasible? *Journal of Child Neurology*. 2008;23(2):192-198. https://doi.org/10.1177/0883073807308716
20. Israilova VK, Abdymoldaeva ZhA, Kulmurat MA. Neuromonitoring (Invos monitor) in patients with stroke. *Vestnik Kazakhskogo natsional'nogo meditsinskogo universiteta*. 2015;4:343-346. (In Russ.).
21. Goitein KJ, Amit Y, Mussaffi H. Intracranial pressure in central nervous system infections and cerebral ischaemia of infancy. *Archives of Disease in Childhood*. 1983;58(3):184-186. https://doi.org/10.1136/adc.58.3.184
22. Møller K, Larsen FS, Qvist J, Wandall JH, Knudsen GM, Gjørup IE, Skinhøj P. Dependency of cerebral blood flow on mean arterial pressure in patients with acute bacterial meningitis. *Critical Care Medicine*. 2000;28(4):1027-1032. https://doi.org/10.1097/00003246-200004000-00019
23. Paulson OB, Brodersen P, Hansen EL, Kristensen HS. Regional cerebral blood flow, cerebral metabolic rate of oxygen, and cerebrospinal fluid acid-base variables in patients with acute meningitis and with acute encephalitis. *Acta Medica Scandinavica*. 1974;196(3):191-198. https://doi.org/10.1111/j.0954-6820.1974.tb00994.x
24. Tariq A, Aguilar-Salinas P, Hanel RA, Naval N, Chmayssani M. The role of ICP monitoring in meningitis. *Neurosurgical Focus*. 2017;43(5):E7. https://ddoi.org/10.3171/2017.8.FOCUS17419
25. Oshorov AV, Goryachev AS, Popugaev KA, Polupan AA, Savin IA, Lubnin AYu. Monitoring of cerebral perfusion pressure in intensive care (literature review). *Vestnik anesteziologii i reanimatologii*. 2013;10(2):052-059. (In Russ.).
26. Goldstein B, Giroir B, Randolph A; International Consensus Conference on Pediatric Sepsis. International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatric Critical Care Medicine*. 2005;6(1):2-8. https://doi.org/10.1097/01.PCC.0000149131.72248.E6
27. McIntosh AM, Tong S, Deakyne SJ, Davidson JA, Scott HF. Validation of the vasoactive-inotropic score in pediatric sepsis. *Pediatric Critical Care Medicine*. 2017;18(8):750-757. https://doi.org/10.1097/PCC.0000000000001191
28. Aleksandrovich YuS, Pshenisnov KV. Application inotropic and vasoactive drugs in critical conditions newborns. *Rossijskij vestnik detskoj khirurgii, anesteziologii i reanimatologii*. 2011;3:106-112. (In Russ.).
29. Likhvantsev VV, Yadgarov MYa, Berikashvili LB, Kadantseva KK, Kuzovlev AN. Sample size estimation. *Anesteziologiya i Reanimatologiya*. 2020;(6):77-86. (In Russ.). https://doi.org/10.17116/anaesthesiology202006177
30. Kuzovlev AN, Yadgarov MYa, Berikashvili LB, Ryabova EV, Goncharova DD, Perekhodov SN, Likhvantsev VV. Choosing the right statistical test. *Anesteziologiya i Reanimatologiya*. 2021;(3):88-93. (In Russ.). https://doi.org/10.17116/anaesthesiology202103188
31. Vasilyeva YuP, Skripchenko NV, Klimkin AV, Bedova MA, Levina OA, Ostapenko BV. A comprehensive structural and functional approach to non-invasive diagnosis of intracranial hypertension and its degree in meningitis and encephalitis in children. *Prakticheskaya meditsina*. 2022;20(1):56-66. (In Russ.). https://doi.org/10.32000/2072-1757-2022-1-56-66
32. Dong J, Li Q, Wang X, Fan Y. A review of the methods of non-invasive assessment of intracranial pressure through ocular measurement. *Bioengineering*. 2022;9(7):304. https://doi.org/10.3390/bioengineering9070304
33. Li J, Wan C. Non-invasive detection of intracranial pressure related to the optic nerve. *Quantitative Imaging in Medicine and Surgery*. 2021;11(6):2823-2836. https://doi.org/10.21037/qims-20-1188
34. Andreytseva MI, Petrikov SS, Khamidova LT, Solodov AA. Ultrasound examination of the structures of the optic nerve canal in the diagnosis of intracranial hypertension in patients with intracranial hemorrhages. *Zhurnal im. N.V. Sklifosovskogo. Neotlozhnaja meditsinskaya pomoshch'*. 2018;7(4):349-356. (In Russ.). https://doi.org/10.23934/2223-9022-2018-74-349-356
35. Philip S, Chaiwat O, Udomphorn Y, Moore A, Zimmerman JJ, Armstead W, Vavilala MS. Variation in cerebral blood flow velocity with cerebral perfusion pressure >40 mm Hg in 42 children with severe traumatic brain injury. *Critical Care Medicine*. 2009;37(11):2973-2978. https://doi.org/10.1097/CCM.0b013e3181a963f6
36. Grände PO, Nordström CH. Management of CPP/ICP: The Lund concept. *European Journal of Anaesthesiology*. 1998;15:42-43.
37. Singh Y, Villaescusa JU, da Cruz EM, Tibby SM, Bottari G, Saxena R, Guillén M, Herce JL, Di Nardo M, Cecchetti C, Brierley J, de Boode W, Lemson J. Recommendations for hemodynamic monitoring for critically ill children-expert consensus statement issued by the cardiovascular dynamics section of the European Society of Paediatric and Neonatal Intensive Care (ESPNIC). *Critical Care*. 2020;24(1):620. https://doi.org/10.1186/s13054-020-03326-2
38. Rosner MJ, Rosner SD, Johnson AH. Cerebral perfusion pressure: management protocol and clinical results. *Journal of Neurosurgery*. 1995;83(6):949-962. https://doi.org/10.3171/jns.1995.83.6.0949

Received 31.01.2023
Accepted 28.03.2023