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FEATURES OF NONINVASIVE CEREBRAL OXIMETRY AND CENTRAL HEMODYNAMICS IN YOUNG CHILDREN WITH HYDROCEPHALUS

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Abstract. *Features of noninvasive cerebral oximetry and central hemodynamics in young children with hydrocephalus. Pavlysh O.S., Snisar V.I. Hydrocephalus is one of the most common diseases of the nervous system in young children. Features of structural and morphological changes of the brain in children with hydrocephalus are the predominance of signs of periventricular ischemia of brain tissue due to cerebral circulatory disorders. Despite the existence of a large number of methods for assessing cerebral hemodynamics, in the modern literature there is only limited information about the oxygen status of the brain when using different types of anesthesia in children. The aim of the study was to assess the dynamics of noninvasive cerebral oximetry and central hemodynamics in young children with hydrocephalus during ventriculoperitoneal shunting. The research included 59 young children with acquired hydrocephalus who underwent ventriculoperitoneal shunting. 34 children underwent total intravenous anesthesia with propofol, 25 children – total inhalation anesthesia with sevoflurane. Intraoperative control of vital functions of the patient was performed: systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, regional saturation, carbon dioxide level on exhalation, sevoflurane concentration on inspiration and exhalation, non-invasive cerebral indicators. Children with acquired hydrocephalus had cerebral oximetry within normal regional level. The use of sevoflurane leads to increased cerebral oxygenation by inhibiting cerebral metabolic needs for oxygen and vasodilation of blood vessels with increased cerebral blood flow. Total intravenous anesthesia does not change the rate of intraoperative cerebral oxygenation, leads to hemodynamic changes in the form of decreased stroke volume, which may indicate that propofol reduces the level of oxygen consumption by the brain with decreased cerebral blood flow against the background of hemodynamic inhibition.*

Резюме. *Особливості показників неінвазивної церебральної оксиметрії та центральної гемодинаміки в дітей раннього віку з гідроцефалією. Павлиш О.С., Снісарь В.І. Гідроцефалія є одним з найбільш поширених захворювань нервової системи в дітей раннього віку. Особливостями структурно-морфологічних змін головного мозку в дітей з гідроцефалією є переважання ознак перивентрикулярної ішемії мозкової тканини за рахунок порушення мозкового кровообігу. Незважаючи на існування великої кількості методів оцінки церебральної гемодинаміки, у сучасній літературі є лише обмежені відомості про показники кисневого статусу головного мозку під час використання різних видів анестезії в дітей. Метою роботи була оцінка динаміки показників неінвазивної церебральної оксиметрії та центральної гемодинаміки в дітей раннього віку з гідроцефалією при проведенні вентрикулоперитонеального шунтування. У дослідження було включено 59 дітей раннього віку з набутою формою гідроцефалії, котрим проводилось вентрикулоперитонеальне шунтування. У 34 дітей була проведена тотальна внутрішньовенна анестезія пропофолом; у 25 дітей – тотальна інгаляційна анестезія севофлюраном. Інтраопераційно виконувався контроль життєво важливих функцій пацієнта: систолічного артеріального тиску, діастолічного артеріального тиску, середнього артеріального тиску, частоти серцевих скорочень, регіонарної сатурації, рівня вуглекислого газу на видиху, концентрації севофлюрану на вдиху й видиху, показники неінвазивної церебральної оксиметрії. У дітей з набутою гідроцефалією показники церебральної оксиметрії знаходяться на рівні регіонарної норми. Використання севофлюрану призводить до підвищення церебральної оксигенації за рахунок пригнічення церебральних метаболічних потреб у кисні та вазодилатації судин з підвищенням мозкового кровотоку. Тотальна внутрішньовенна анестезія не змінює показники інтраопераційної церебральної оксигенації, призводить до гемодинамічних змін у вигляді зменшення ударного об'єму, що може свідчити про те, що пропофол зменшує рівень споживання кисню головним мозком зі зниженням мозкового кровотоку на тлі пригнічення гемодинаміки.*

Hydrocephalus is one of the most common diseases of the nervous system in young children. It is found in 0.1-2.5% of newborns and 30-40% of children with perinatal lesions of the central nervous system [7]. Peculiarities of structural and morphological changes of the brain in children with hydrocephalus are the predominance of signs of periventricular ischemia of brain tissue due to cerebral circulatory disorders on the background of ventriculomegaly [9]. That is why children with acquired hydrocephalus develop oxygen deficiency due to persistent vasospasm, which leads to a decrease in adenosine triphosphate (ATP) production during oxidative phosphorylation. One of the leading methods of surgical treatment is ventriculoperitoneal shunting, and the main goal during anesthesia is to maintain adequate perfusion pressure, as well as maintaining the optimal level of oxygenation of the brain [5].

Despite a large number of methods for assessing cerebral hemodynamics, in the modern literature there is a little information about the oxygen status of the brain while using different types of anesthesia [15]. First of all, the process of oxygen delivery to brain tissues is complex, multicomponent and depending on many indicators (systemic and regional hemodynamics, blood oxygen capacity, metabolic needs); secondly, currently available methods for estimating oxygen status parameters are either too huge to use in the operating room, or invasive, which made limits in their use for everyday practice.

Currently, the method of cerebral oximetry near-infrared reflectance spectroscopy (NIRS) is being actively implemented, the main advantages of which are informativeness, noninvasiveness and safety. In complex settings such as pediatric cardiac surgery, pediatric neurosurgery, pediatric and neonatal intensive care, NIRS is increasingly used to detect episodes of cerebral ischemia, both during surgery and in the post-operative period. Cerebral NIRS devices measure the average oxygen saturation of tissue (rSO_2) and, also, reflect the saturation of hemoglobin with oxygen from venous, capillary and arterial blood. Based on multiple studies, most NIRS clinical devices suggest venous-arterial distribution in cortical tissue – 70/30% [14]. As a result, changes in rSO_2 largely reflect changes in venous blood oxygen saturation.

Detection of low cerebral oxygenation during anesthesia in children, as well as related physiological factors such as hypotension and hypoxemia, could improve the safety of anesthesia, because these mechanisms may be the cause of neurological damage. However, currently there are insufficient clinical data on the critical levels of measurable variables that are necessary for the safe management of the perioperative period of patients inclined to cerebral ischemia [6].

The aim of the study was to assess the dynamics of noninvasive cerebral oximetry and central hemodynamics in young children with hydrocephalus when using total intravenous anesthesia with propofol and inhalation anesthesia with sevoflurane during ventriculoperitoneal shunting.

MATERIALS AND METHODS OF RESEARCH

The research included 59 children aged 2.0 ± 1.4 years with an acquired form of hydrocephalus, who underwent ventriculoperitoneal shunting on the basis of ME «Dnipropetrovsk Region Children's Clinical Hospital» Dnipropetrovsk Regional Council», Ukraine for 2018-2019. The physical status of the patients matched to the level of ASA-II [11]. Total intravenous anesthesia (TIVA) with mechanical lung ventilation (propofol + fentanyl + rocuronium) was performed in 34 children. The rest 25 children received inhalation anesthesia (IA) with sevoflurane (sevoflurane + fentanyl + rocuronium).

The research was conducted in accordance with the principles of bioethics set out in the WMA Declaration of Helsinki – “Ethical principles for medical research involving human subjects” and “Universal Declaration on Bioethics and Human Rights” (UNESCO).

Premedication consisted of intravenous atropine 0.01-0.015 mg/kg and dexamethasone 0.15 mg/kg. Propofol in our study was used in a standard dose (induction of 3-5 mg/kg, maintenance of anesthesia by infusion of 8-12 mg/kg/h) [4]. Inhalation anesthesia with sevoflurane was performed according to the method of low flow anesthesia [10]. Induction began with a concentration of 1.5 minimum alveolar concentrations (MAC) followed by a transition to a low flow of oxygen-air mixture of 1.0 l/min (FiO_2 -40-50%) and an anesthetic content of 0.6-0.8 MAC. In both groups, mechanical lung ventilation was performed in the mode of normoventilation, with the support of End-tidal CO_2 in the range of 34-38 mm Hg. Depth of anesthesia was monitored by bispectral index (BIS, Aspect Medical Systems, USA). During intraoperative period the monitor UM-300 (UTAS, Ukraine) was using for performing control of vital functions of the patient: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), regional saturation (SpO_2) and End-tidal CO_2 ($EtCO_2$), concentrations of sevoflurane on inhalation and exhalation ($FiSev$, $EtSev$) [13]. Noninvasive cerebral oximetry parameters (rSO_2) were measured with the NONIN X-100M (Nonin Medical, Inc. USA). Indicators of stroke volume (SV), cardiac output (CO), systemic vascular resistance (SVR) were determined by the calculation methods [2]. The study included 5 stages: initial (1), induction (2), tracheal intubation (3), traumatic stage of surgery (4), awakening (5).

The values obtained in the control group were used as a starting point for comparison, as physiologically normal values. The statistical processing of the received data was conducted with STATISTICA® 10.0 (StatSoft Inc., license no. STA999K347156-W). For a distribution other than normal, the nonparametric Mann-Whitney test was used. Spearman's rank correlation coefficient was calculated to identify relationships between quantitative variables. The analysis of the dynamics of quantitative indicators was performed on the basis of nonparametric Wilcoxon signed-rank test. To take $p < 0.05$ as the confidence level of the statistical indicators [1].

RESULTS AND DISCUSSION

In children with acquired hydrocephalus, the analysis of cerebral oximetry at baseline showed rSO_2 values averaging $75.5 \pm 1.8\%$. In both groups, and in comparison with the control group, no significant differences in the initial values were observed. The lack of difference with the control group of the initial rSO_2 data can be explained by the fact that prolonged hypoperfusion of the cerebral substance caused by vascular spasm, combined with compression of the distended ventricles of the brain leads to disruption of membrane oxygen transport and venous outflow from the brain. This is confirmed by the fact that in the brain of children with hydrocephalus the level of glucose metabolism increases due to increased anaerobic glycolysis, regardless of the level of cerebral blood flow [8].

In its turn, the analysis of the primary condition of the cardiovascular system and in comparison with the control group, in children with acquired hydrocephalus revealed a significant increase in SV, CO by 18.5% and 28.2%, accordingly, and decrease of SVR by 25.1% (Table 1), which was regarded as a hyperkinetic variation of hemodynamics. On the one

hand, this can be explained by the compensatory mechanism of the physiological decrease in SVR in response to increased output of blood discharge. Another explanation for this is that it remains unclear which of the components of CO is most important for maintaining cerebral perfusion pressure (CPP). It is possible that the stroke volume is most important for cerebral blood flow. This assumption is based on the model "Windkessel" [3], when at sufficient systemic pressure in systole, the capacitive vessels are filled with blood, while the vessel wall expands. In this case, the energy needed to maintain cerebral blood pressure in diastole accumulates. Based on this model, this change in the relationship of hemodynamic parameters can be explained as follows: in conditions of moderate intracranial hypertension, when autoregulation of cerebral blood flow is intense and centralization of blood circulation is not effective, increased cardiac output supports the systolic component of CPP.

After analyzing the dynamics of cerebral oxygenation a significant increase by 15.9% ($p < 0.05$) in the IA group on the second stage in comparison with the initial level (Table 2) was noted. This is explained that all inhaled anesthetics cause cerebral vasodilation (direct effect) by acting directly on the smooth muscle cells of the vessels of the brain, which leads to a decrease in cerebrovascular resistance and acceleration of cerebral blood flow. However, their indirect inhibition of cerebral metabolism leads to a decrease in cerebral blood flow (indirect effect). The disproportionate decrease in cerebral blood flow with a decrease in oxygen consumption by the brain is explained by the fact that the direct effect of vasodilation when using sevoflurane, partially counteracts the decrease in cerebral blood flow with a decrease in cerebral metabolism [12].

Table 1

Initial hemodynamic parameters in children with hydrocephalus ($M \pm m$)

Parameters	Group TIVA (n=34)	Group IA (n=25)	Control (n=20)
HR (b/min)	121.9±16.4	127.3±19.2	114.00±20.08
SBP (mm Hg)	92.8±6.6	92.2±9.8	96.00±7.8
DBP (mm Hg)	57.1±4.9	57.0±7.08	62.90±6.2
MAP (mm Hg)	69.0±5.0	68.7±7.5	74.50±14.1
SV (ml)	31.11±5.48*	28.2±4.85*	25.21±2.4
CO (l/min)	3.76±0.65*	3.57±0.71*	2.87±0.98
SVR (D/s/cm ⁵)	1513.59±277.89*	1613.22±416.15*	2076.65±593.87

Note. * $p < 0.05$ compared with the control group.

High levels of rSO₂ remain in all subsequent stages (Table 2), this shows that sevoflurane, even at a concentration of 0.6-0.8 MAC, causes significant inhibition of cerebral metabolic needs for O₂ and maintains high cerebral blood flow, in contrast to the TIVA group, where we recorded the stability of intraoperative rSO₂. Under physiological conditions,

to maintain a constant level of O₂, the body can either increase oxygen extraction by tissues and/or increase cardiac output. In the case of is decreased oxygen consumption, its extraction by tissues is proportionally reduced, which should also be reflected in an increase of rSO₂ indices.

Table 2

Parameters of cerebral oximetry in children with hydrocephalus(M±m)

	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Group TIVA					
rSO ₂ (%)	75.2±1.8	75.8±1.4*	77.6±1.5*	78.0±1.2*	77.6±2.0*
Group IA					
rSO ₂ (%)	75.9±1.7	88.0±4.6*#	87.8±4.1*#	84.9±4.0*#	80.7±3.8*#

Note: * p<0.05 comparing between groups; # p<0.05 compared to the initial stage.

The vasodilatory effect of sevoflurane in small concentrations is characterized by a significant dose dependence and regional features of the vascular bed, while deep anesthesia causes a sharp generalized dilatation of arterioles and venules. The most pronounced hemodynamic effect of halogen-containing anesthetics is a decrease in blood pressure. Meanwhile, in the IA group, starting from the 2nd stage, there is a slow drop in blood pressure. The dynamics of blood pressure indicates that at stage 4

SBP was less by 3.6% (p<0.05), DBP – by 5.9% (p<0.05) and MAP – by 4.9% (p<0.05) from baseline.

This was indeed due to a decrease by 13.7% of the SVR from the initial value (p<0.05) at the stage 4. Against the background of a decrease in SVR and an increase in heart rate, there was an increase in SV (Fig. 1) and CO (by 7.1% and 10%, respectively), which remained elevated at all stages of anesthesia with sevoflurane (p<0.05).

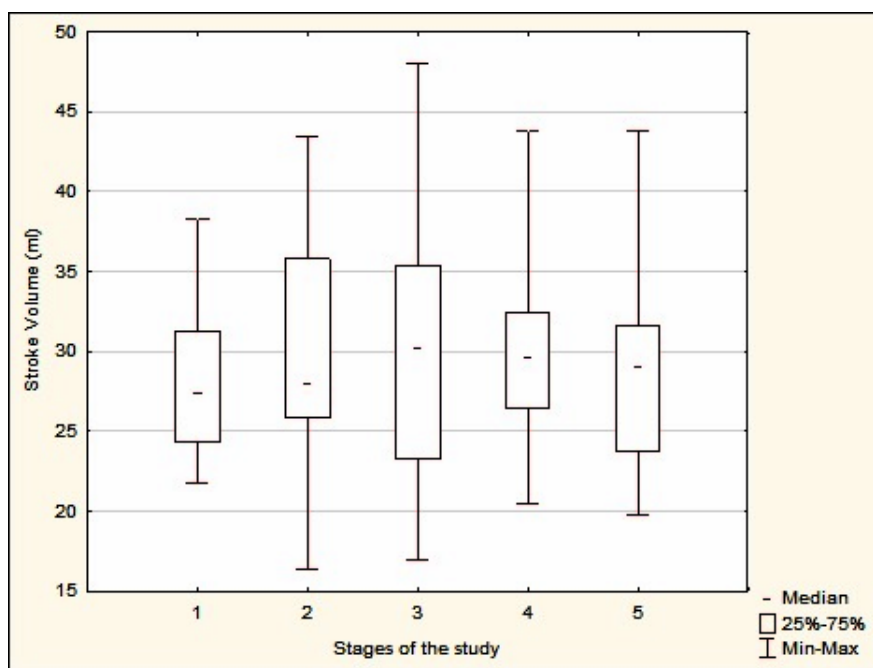


Fig. 1. Dynamics SV(ml.) in the group IA

At the same time, it is known that propofol also lowers blood pressure. The dominant effect of propofol is considered to be a decrease in peripheral vascular resistance, leading to the deposition of blood, which is realized through endothelial nitric oxide and a deficiency of sympathetic efferent flow

from the CNS. Dilatation of peripheral vessels leads to a decrease in venous return and a decrease in cardiac output. In the TIVA group up to stage 5 there is a decrease in SV (Fig. 2) by 5.9% from baseline ($p < 0.05$) with minor changes in SBP and MAP.

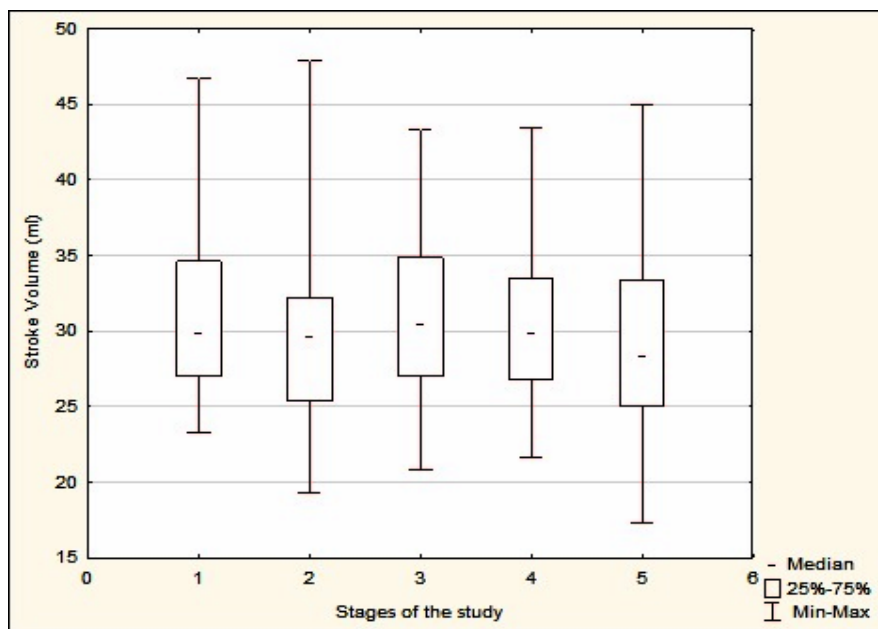


Fig. 2. Dynamics of SV (ml) in the TIVA group

The CO initially increased at the second stage (although not significantly) by 0.8% from the initial level, due to the chronotropic component. In dynamics, the maximum decrease by 5.4% and 6.6% of the initial level of CO was observed in the fourth and fifth stages of the study ($p < 0.05$). A significant increase in the dynamics of SVR by 4.4% and 7.0% at these stages indicated that in children with hydrocephalus, on the background of anesthesia with propofol, maintenance of CO is due to increased afterload.

CONCLUSIONS

1. In children with acquired hydrocephalus, against the background of hyperkinetic variant of central hemodynamics and hypoperfusion of the cerebral substance, cerebral oximetry is within normal limits.

2. The use of sevoflurane leads to low arterial pressure by reducing systemic vascular resistance, increasing cardiac output, and a significant increase in cerebral oxygenation by suppressing cerebral metabolic needs for O_2 and vasodilation of blood

vessels with increased cerebral blood flow. The vasodilatory effect of sevoflurane is maintained at all stages of anesthesia.

3. Total intravenous anesthesia with propofol leads to hemodynamic changes in the form of a decrease in stroke volume (due to venous dilatation), which can be compensated by an increase in systemic vascular resistance, in order to maintain cardiac output.

4. Unlike sevoflurane, the use of propofol maintains the stability of intraoperative rSO_2 , which may indicate that propofol reduces oxygen consumption by the brain with a decrease in cerebral blood flow against the background of hemodynamic inhibition, which depletes compensatory mechanisms and further reduces cardiac output can cause potentially dangerous disturbances of cerebral hemodynamics and damage of brain substance due to ischemia.

Conflict of interests. The authors declare no conflict of interest.

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