OXYGEN PROVISION OF THE BRAIN AT VARIOUS STAGES OF OPERATION IN PATIENTS WITH CHRONIC PULMONARY ARTERY THROMBOEMBOLISM

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The authors studied cerebral oxygen supply by means of cerebral oximetry in patients presenting with chronic pulmonary artery thromboembolism (PATE) at various stages of operation. The study was aimed at assessing cerebral oxygen supply while carrying out surgical treatment in patients with chronic PATE on the background of various methods of perfusion. Thromboendarterectomy (TEA) from the pulmonary artery with the use of circulatory arrest and craniocerebral hypothermia is accompanied by more pronounced impairment of oxygen supply of the brain with a decrease in the cerebral oxygenation indices by more than 30% from the baseline values. These alterations promote increased risk for the development of neurological complications in the early postoperative period. Using the technique of antegrade cerebral perfusion ensures a minimum decrease of cerebral oxygenation during TEA and contributes to a reduction of the risk for the development of neurological complications.

Key words: *cerebral oxygenation, pulmonary artery thromboembolism.*

Chronic pulmonary artery thromboembolism (hereinafter referred to as PATE) is one of the most severe complications of acute PATE. The probability of normalization of pulmonary circulation and the function of the right portions of the heart within the subsequent terms is utterly low. A promising surgical method of treatment for this disease is thromboendarterectomy (TEA) from the branches of the pulmonary artery (PA) [1, 2]. Prevention of impaired cerebral circulation during TEA from the PA branches is currently important since it radically influences the quality of life of those having endured the intervention. The main damaging agent in the mechanism of formation of impaired cerebral circulation is hypoxia of brain neurons followed by ischaemic lesion of cellular structures [3]. The underlying factors are both initial hypoxia and exacerbation of hypoxia of cerebral tissues during surgical treatment, resulting from long-term artificial perfusion, hypothermia, and the use of circulatory arrest (CA) [4, 5]. Patients requiring hypothermic CA accompanied by discontinuation of cerebral circulation in the brain have the highest risk for the development of cerebral ischaemia and severe neurological complications [6, 7]. Currently, there exist alternative methods of carrying out surgical interventions with the use of artificial circulation (AC) [8, 9]. Specialists of the Novosibirsk Scientific Research Institute of Circulatory Pathology named after Academician E.N. Meshalkin under the RF Ministry of Public Health clinically implemented a method of performing TEA from the PA under the conditions of moderate hypothermia with unilateral antegrade cerebral perfusion (UACP). This method is one of the most important trends of preventing postoperative neurological complications, yielding good results while carrying out reconstructive operations on the aortic arch [10].

The study was aimed at assessing oxygen supply of the brain while carrying out surgical treatment in patients presenting with chronic PATE on the background of various methods of perfusion.

MATERIALS AND METHODS

The study comprised a total of forty 39-to-54-year-old (mean age 48 years) patients diagnosed as having chronic PATE, chronic post-embolic pulmonary hypertension (CPEPH) and admitted for surgical treatment at the Novosibirsk Scientific Research Institute of Circulatory Pathology named after Academician E.N. Meshalkin. The diagnosis was verified by the findings of angiopulmonography with the assessment the level of pressure in the PA (mm Hg), resistance of vessels of minor circulation (din×s×cm^{-5}). We carried out lung perfusion scintigraphy, MSCT angiography of PA branches. The scope of embolic lesion was assessed in points according to the method suggested by Miller [11]. Of the 40 patients, there were 28 (70%) men and 12 (30%) women. The average duration of the disease amounted to 3 (range 1.3–4.1) years. All patients were subjected to surgical treatment in the scope of TEA from PA branches. We did not include into the study patients with haemodynamically significant lesions of brachiocephalic and intracranial arteries, with moderate or severe neurological disorders prior to operation, with a history of acute cerebral circulation impairments. The findings of transcranial dopplerography revealed closed circle of Willis.

Oxygen supply of the brain was evaluated by means of bilateral transcranial spectroscopy [INVOS 5100 (Somanetics, USA)]. We determined the level of cerebral oxygenation (rSO_2, %) of the right and left hemispheres, calculating the index of haemodynamic conformity (IHC) by for the hemispheres – correspondence of oxygen supply to metabolic requirements of the brain (IHC, arbitrary units), which is the ratio of rSO_2 to the level of mean arterial pressure (AP_{mean}) amounting in the norm to more than 0.75 [12]. During the study, the sensor was applied onto the right and left frontotemporal regions. Cerebral oximetry consists in measuring the degree of light absorption within the range varying from 700 to 1000 nm, travelling through biological objects. Within the limits of this range, the only biological substances possessing oxygen-dependent spectra of absorption are haemoglobin and cytochromoxidase. Therefore, this method makes it possible to evaluate the oxygen status of haemoglobin present in the vessels of the region of the brain under study. It is known that venous vessels account for 85% of the total volume of the cerebral vascular bed [13]. From this it follows that the method of cerebral oximetry makes it possible to assess saturation of haemoglobin with O_2 predominantly in blood of cerebral venous vessels in order to evaluate the degree of cerebral ischaemia. The normal values of rSO_2 correspond to the normal values of central venous saturation, i. e. 63–75% [14]. This method is non-invasive, making it possible to obtain real-time data.

Cerebral oxygenation of the left and right hemispheres was registered at various stages of operation, including: initial narcosis, artificial circulation (AC), cardiac arrest (CA) or unilateral antegrade cerebral perfusion (UACP) during TEA from the PA branches, period of warming on the background of AC, and the end of the operation. At early terms after surgery we assessed postoperative neurological complications with due regard for the method of perfusion during TEA from the PA branches.

Surgical treatment of patients was carried out under conditions of AC in the nonpulsatile mode. The volumetric perfusion rate was maintained at a level of 2.5 $l/(min \times m^2)$. The gas blood composition during cooling was maintained according to the alpha-stat technique. All patients were subdivided into two groups. Group One (n=25) was composed of patients subjected to operative treatment under conditions of moderate hypothermia (25°C) with the conduction of UACP at the volumetric velocity of 10 $ml/(kg \times min)$. Group Two (n=15) consisted of patients undergoing perfusion cooling of the body to 20°C, craniocerebral hypothermia (surrounding of the patient's head with ice) with CA at the stage of TEA. In Group One patients after TEA from the left PA we began the stage of reperfusion with an increase of the volumetric velocity of the blood flow to the estimated one, which by duration amounted to 50% of the UACP time. We then again performed UACP during the period of TEA from the right PA. Patients of Group Two were also subjected to reperfusion at the full estimated velocity with the duration of 50% of the CA time. The main stage of the operation was followed by warming of the patient.

All patients underwent the standard perioperative monitoring including continuous pulse oximetry, registration of ECG, heart rate (HR), arterial and central venous pressure. At various stages of the operation we determined the gas composition of arterial and venous blood. For the analysis we used the following data: PCO_2 – partial pressure of carbon dioxide in blood, PO_2 – partial pressure of oxygen in blood, O_2SAT – oxygen saturation of blood. We also analysed the concentration of total blood haemoglobin (tHb), haematocrit (Hct), haemodynamic parameters: mean arterial pressure ((systolic AP – diastolic AP)/ 3 + diastolic AP), minute volume of circulation (l/min).

The statistical analysis of the obtained findings was carried out using the package of statistical programmes Statistica version 6.0 (USA). The data are represented as the median (25–75%), Me (Q_{25}–Q_{75}). Significance of differences of dependent values was determined according to the Wilcoxon criterion, and that of independent values by the Mann–Whitney rank test criterion. Interdependence of the parameters was compared using the Spearman's rank correlation coefficient. Differences were regarded statistically significant if $p<0.05$.

RESULTS

Table 1 shows the data of rSO_2 of cerebral hemispheres and the index of haemodynamic conformity (IHC) in patients with chronic PATE of the both groups at various stages of operation.

As can be seen from Table 1, while in the norm rSO_2 of cerebral hemispheres varied from 63 to 75%, in patients with chronic PATE the parameters of rSO_2 of cerebral hemispheres were decreased at the stage of initial narcosis, with the IHC values being also below the norm, thus suggesting a decrease in the baseline indices of oxygen supply of the brain in this cohort of patients.

At the stage of AC, patients of the both groups despite the effect on anaesthesia and the temperature mode, promoting decreased metabolic requirement of the brain, showed no significant increase in the rSO_2 parameter, which may be related to haemodilution. Group One patients at the stage of TEA with UACP were found to have a decrease in the rSO_2 of the left and right hemispheres by 16 and 18%, respectively in relation to the previous indices during AC ($p<0.05$). Group Two patients with the use of hypothermic CA and craniocerebral hypothermia during TEA demonstrated a

Table 1

Cerebral oxygenation in patients with chronic pulmonary artery thromboembolism at various stages of surgical treatment

Parameters, unit of measurement	Initial narcosis		Beginning of artificial circulation		Minimal value of rSO_2 at the stage of TEA		Complete warming		End of operation	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Right ventricle rSO_2, %	58,0 (50–64)	55,0 (50–59)	64,0 (58–69)	59,0 (51–63)	50 (43–56)	43 (41–51)	72,0 (55–79)	59,5* (53–60)	62,0 (51–70)	58,0 (47–65)
IHC of the right hemisphere, arbitrary unit	0,67 (0,59–0,81)	0,63 (0,52–0,70)	0,87 (0,77–1,03)	0,84 (0,65–0,92)	–	–	0,87 (0,72–1,02)	0,83 (0,72–0,92)	0,81 (0,71–1,01)	0,64 (0,59–0,76)
Left ventricle rSO_2, %	61,0 (56–66)	56,0 (52–61)	67,0 (60–74)	55,5 (52–67)	49 (45–61)	36* (34–38)	71,0 (54–79)	51,0* (49–59)	61,0 (53–70)	57,0 (47–62)
IHC of the left hemisphere, arbitrary unit	0,71 (0,61–0,86)	0,59 (0,54–0,72)	0,92 (0,80–1,14)	0,79 (0,66–0,84)	–	–	0,91 (0,67–1,08)	0,86 (0,71–0,94)	0,83 (0,73–1,0)	0,71 (0,65–0,81)

Notes: rSO_2 – cerebral oxygenation; IHC – index of haemodynamic conformity; TEA – thromboendarterectomy.

more pronounced decrease in the oxygen supply of the brain with significant difference for the left hemisphere ($p<0.05$). The maximum decrease in the rSO_2 of the right and left hemisphere amounted to 27 and 35%, respectively ($p<0.05$).

Hence, in Group One patients the maximal decrease of rSO_2 indices during TEA din not exceed 20%, in Group Two patients the decrease of this index amounted to 35% as compared with the baseline values. After the end of TEA and connection of AC at the stage of warming the rSO_2 of the right and left hemispheres in Group One patient exceeded the initial values and in Group Two patients these parameters were significantly lower than in Group One patients ($p<0.05$). At the end of the operation the groups did not differ by the rSO_2 of the both hemispheres ($p<0.05$).

Analysing the correlations between rSO_2 and perioperative indices of the blood gas composition revealed direct interrelationship between rSO_2 and CO_2 partial pressure in arterial blood at the stage of the initial narcosis ($r=0.43$; $p<0.05$). The detected direct relationship between rSO_2 and O_2 partial pressure level in venous blood ($r=0.46$; $0<0.05$), as well as between rSO_2 and oxygen saturation of venous blood during AC ($r=0.45$; $p<0.05$) is explained by the fact that blood passing through the brain is venous by 85%. This fact reflects reasonableness and feasibility of using cerebral oximetry as monitoring of adequate perfusion in cardiosurgical patients [15]. Hence, at the stage of initial narcosis with relatively preserved autoregulation of cerebral blood flow the leading factor influencing the values of cerebral oxygenation is the level of CO_2 of arterial blood. During AC the values of cerebral oxygenation correlate with the main determinants of oxygen transport, which is necessary for maintaining adequate oxygen supply of the brain at various stages of operation.

Table 2 shows the laboratory indices of blood and haemodynamics of the both groups of patients at various stages of operation.

During AC all patients showed a decrease in total haemoglobin, haematocrit as compared with the indices at the stage of initial narcosis ($p<0.05$), which is conditioned by haemodilution on the background of cooling. The dynamics after the end of TEA from the PA branches on the background of warming showed a statistically significant decrease in the O_2 partial pressure of venous blood, which characterises an increase in the O_2 uptake on the background of whole-body warming ($p<0.05$). The average partial pressure was maintained at a level not below 70 mm Hg at all stages of operation.

A decrease in the inflow of blood to the brain (resulting from the drop of systemic arterial pressure) leads to disruption of cerebral haemodynamics and impaired cerebral circulation resulting in ischaemia [16]. Analysing the neurological status in the early postoperative period revealed that 46% of Group Two patients with the use of hypothermic CA cardiac arrest and craniocerebral hypothermia during TEA, in whom at the given stage was registered a significant decrease in cerebral oxygenation (to 35%) in relation to the baseline parameters were found to have neurological complications (acute cerebral circulatory insufficiency, moderately manifested dyscirculatory encephalopathy). Acute insufficiency of cerebral circulation detected in 2 patients was registered in the basins of the left and right internal carotid arteries. Moderately manifested dyscirculatory encephalopathy was registered in five patients. In Group One patients with the use of UACP during TEA and a decrease in the rSO_2 indices of the right and left hemispheres at the stage of TEA by not more than 20% of the baseline values at the early postoperative period impairments of the neurological status were registered in only 3 patients (12%) in the form total cerebral neurological syndrome (dizziness, headache, memory disorders). By the anthropometric data, baseline indices of rSO_2 (in the initial period of postoperative monitoring), severity of the baseline condition, duration of AC, as well as occlusion of the aorta, these groups of patients did not differ. Thus,

Table 2

Laboratory data and haemodynamic indices in patients with chronic PATE at various stages of operation

Parameters, unit of measurement		Initial narcosis		Beginning of extracorporeal circulation		Complete warming		Extracorporeal circulation disconnected	
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
PCO_2 (mm Hg)	Artery	36,7 (30,8–38,6)	34,2 (30,5–40,5)	39,2 (36,0–45,6)	38,1 (33,3–45,7)	34,1 (31,7–40,6)	34,1 (32,0–35,8)	35,8 (32,5–39,6)	34,8 (33,7–39,6)
	Vein	–	–	45,1 (41,2–47,2)	39,9 (37,3–41,1)	32,3 (29,4–38,3)	33,1 (29,1–41,2)	34,9 (30,8–38,9)	32,8 (30,7–38,1)
PO_2 (mm Hg)	Artery	189,7 (117,9–267,8)	179,0 (172,4–224,4)	267,7 (114,1–369,4)	151,0 (75,9–304,4)	104,1 (76,6–220,7)	76,3 (54,5–233,7)	224,4 (119,0–278,0)	99,7 (54,5–233,7)
	Vein	–	–	60,0 (54,4–89,9)	54,4 (44,5–70,8)	42,2 (38,9–46,0)	37,9 (34,0–37,8)	45,7 (37,9–49,2)	42,9 (31,1–48,8)
tHb (g/l)	Artery	148,0 (134,0–160,0)	139,0 (137,0–148,0)	107 (90,0–110,0)	109,0 (89,0–116,0)	100,0 (89,0–107,0)	86,0 (72,5–99,0)	98,0 (87,0–106,5)	89,0 (73,0–99,0)
	Vein	–	–	103,0 (97,0–107,0)	108,5 (74,0–116,0)	96,0 (86,0–102,0)	89,0 (70,0–100,0)	99,5 (89,5–106,0)	91,5 (78,0–123,5)
Hct (%)	Artery	44,0 (39,0–47,0)	41,0 (40,0–44,0)	31,0 (29,0–32,0)	32,0 (26,0–34,0)	30,0 (27,0–31,0)	29,0 (22,0–30,0)	29,0 (26,0–31,0)	26,0 (21,0–27,0)
	Vein	–	–	30,0 (29,0–31,0)	31,0 (22,0–34,0)	28,5 (25,0–30,0)	25,5 (21,0–29,0)	30,0 (27,0–31,0)	27,0 (23,0–36,5)
O_2SAT (%)	Artery	99,3 (98,5–99,6)	99,3 (99,1–99,5)	99,6 (98,1–99,8)	98,9 (94,6–99,8)	98,7 (96,7–99,6)	98,9 (91,7–99,5)	99,5 (98,7–99,7)	99,5 (99,0–99,7)
	Vein	–	–	91,1 (88,0–97,0)	89,7 (83,3–94,4)	82,7 (79,2–84,1)	73,6 (69,0–78,2)	83,6 (80,2–84,2)	79,4 (57,1–86,1)
AP_{mean} (mm Hg)		85,7 (75,3–98,0)	76,1 (68,3–82,0)	72,8 (61,0–81,6)	69,7 (61,3–82,3)	72,7 (66,5–85,2)	71,2 (59,0–80,0)	72,7 (66,5–74,0)	69,7 (58,6–73,6)
MVC (l/min)		4,2 (4,0–4,9)	4,2 (3,9–4,8)	4,8 (4,6–4,9)	4,7 (4,5–4,9)	5,0 (4,6–5,3)	5,0 (4,7–5,3)	4,1 (4,0–4,5)	4,2 (3,9–4,7)

Note: PCO_2 – partial pressure of carbon dioxide in blood; PO_2 – partial pressure of oxygen in blood; tHb – blood total haemoglobin concentration; Hct – haematocrit; O_2SAT – blood oxygen saturation; APmean – mean arterial pressure (systolic AP – diastolic AP/3 + diastolic AP); MVC – minute volume of circulation.

duration of AC and occlusion of the aorta in Group One and Two patients amounted to 190 min (183–209) and 121 (94–135), as well as 197 (186–215) and 125 (96–142), respectively ($p<0.05$).

DISCUSSION

Cerebral blood flow depends to a considerable degree upon the changes in the CO_2 tension in arterial blood. In the brain, CO_2 is the strongest vasodilating factor. Drop of CO_2 partial pressure to 20 mm Hg decreases the value of cerebral blood flow twofold and hypocarbia of less than 20 mm Hg may lead to pronounced cerebral ischaemia induced by vasoconstriction [16]. In our study, interrelationship between the indices of rSO_2 and CO_2 partial pressure in arterial blood at the stage of initial narcosis is indicative of the possibility to regulate oxygen supply at this stage of operation at the expense of maintaining normocapnia.

A decrease in temperature inhibits cerebral metabolism which at 18ºC amounts to 10% of the level in normothermia, hence, preventing exhaustion of cellular high-energy phosphates and increasing the period of time during which lesions may be reversible [17]. This property of deep hypothermia is the basis for the use of the method of CA at the stage of performing TEA [18]. Cardiac arrest is accompanied and followed by an abrupt drop in arterial pressure in major vessels of the brain. Possibilities of autoregulation in this case are limited. In hypoperfusion especially vulnerable are terminal vascular regions of the brain wherein ischaemia occurs earlier and is more pronounced. This is accompanied and followed by accumulation of CO_2 and an increase of acidosis. Besides, accumulation of suboxidized products induces oedema which in its turn may enhance impairments of cerebral tissue perfusion [19]. Special attention should be paid to a decrease in rSO_2 by 30% and more from the baseline values. Clinical studies showed that absolute values below 40% or a decrease in rSO_2 by more than 30% from the initial value are suggestive of neurological impairments [12]. The findings of our study reflect pathophysiological significance of decreased rSO_2 during CA at the stage of TEA in patients with chronic PATE by more than 30% of the initial values – in this cohort of patients half of the cases demonstrated at the early postoperative period impairments of the neurological status. The method of UACP implemented at our Institute, in the period of TEA makes it possible to refuse deep hypothermia, as well as complete arrest of cerebral blood flow, which substantially reduces the risk of neurological complications on the part of the central nervous system [20].

Thus, thromboendarterectomy in patients with chronic PATE with the use of cardiac arrest and craniocerebral hypothermia is accompanied by more pronounced impairment of cerebral oxygen supply, reflected by a decrease in cerebral oxygenation indices by more than 30% from the baseline values. These alterations contribute to increased risk for the development of neurological complications during the early postoperative period. The use of the technique of antegrade cerebral perfusion with moderate hypothermia promotes the minimal decrease in the oxygen supply of the brain during TEA and considerable reduction of the risk for neurological complications.

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