EFFECT OF CRANIOCEREBRAL HYPOTHERMIC PERFUSION ON METABOLISM OF THE ISCHEMIC BRAIN

V. L. Radushkevich, V. V. Malyshev, and A. A. Aleksanov

UDC 616.831-008.9-02:616-008.922.1-008.64

After acute hypoxia was induced in 58 experiments on dogs intravascular perfusion of the brain was carried out with "extracellular" colloid–salt solution. The biochemical parameters of metabolism were determined in fluid flowing into and out of the brain and in the brain tissue. During acute hypoxia, normothermic and, in particular, hypothermic intravascular perfusion of the brain with colloid–salt solution was shown to reduce the disturbances of metabolic homeostasis.

KEY WORDS: brain; acute hypoxia; perfusion; metabolism.

Previous investigations [1, 2] showed that intravascular cooling of the brain in the terminal state can prolong the period of clinical death.

The object of the present investigation was a dynamic study of the metabolic sequelae of normothermic and hypothermic brain perfusion with "extracellular" colloid–salt solution under conditions of acute hypoxia.

EXPERIMENTAL METHOD

After morphine (10 mg/kg) premedication and under superficial barbiturate anesthesia, in 58 experiments on dogs weighing 10-21 kg the blood vessels are cannulated and the sagittal intracranial sinus was trephined and catheterized (the preparatory period). In the main stage of the experiment, after restoration of the reflex and during continued action of barbiturates, heparin (2 mg/kg body weight) was injected and total exsanguination carried out. During the last agonal inspirations and commencing clinical death, for 5 min the vascular system of the brain was perfused with blood substitute fluid. The solution was injected at the rate of 20 ml/min · kg body weight into both common carotid arteries toward the brain, with partial vascular isolation of the head [1]. After passing through the vascular system of the brain, the solution was withdrawn from the cranial vena cava and external jugular vein.

An extracellularly balanced colloid–salt solution of the following composition was used for perfusion: KCl 0.3 g, $NaHCO_3$ 1.5 g, glucose 1.2 g, insulin 2 units, γ-hydroxybutyric acid 1 g, heparin 0.3 ml, rheopolyglucin 290 ml, gelatinol 660 ml, and water to 1 liter.

Perfusion in series I (24 experiments) was normothermic (37.2 ± 0.3°C) and in series II (34 experiments) it was hypothermic (4.5 ± 0.6°C).

The values of pH, pCO_2, and pO_2 were determined (micro-Astrup apparatus, from Radiometer, Denmark) in the original perfusion fluid and also in fluid flowing from the brain after 1, 3, and 5 min and the temperature of the solution, the concentrations of lactate and pyruvate (using chemical reagents from Boehringer, West Germany), and the concentrations of potassium and sodium ions (with a Flaphacol photometer, East Germany) were estimated. The arteriovenous oxygen difference ($A\text{-}Vp O_2$) and the veno-arterial CO_2 difference ($V\text{-}Ap CO_2$) and the lactate/pyruvate ratio were calculated.

In the cerebral cortex the partial oxygen pressure (pO_2) was determined on a PA-3 polarograph and the overall redox potential (RP) was determined amperometrically on the pH-340 apparatus. The data were expressed in percentages and millivolts respectively relative to the initial level (pO_2 100%, RP 0 mV).

Department of General Surgery and Central Research Laboratory, Irkutsk Medical Institute.
(Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 87, No. 5, pp. 410-412, May, 1979. Original article submitted March 30, 1978.

 0007-4888/79/8705-0418$07.50

TABLE 1. Changes in Metabolic Indices during Perfusion (M ± m)

Parameter	Statistical index	Series	Original perfusion fluid	Perfusion fluid flowing out of brain		
				1st minute	3rd minute	5th minute
pO_2, mm Hg		Hypothermia	142,6±0,7	87,6±5,6	108,4±5,4	121,8±4,3
	P_1			<0,001	<0,001	<0,001
	P_2		<0,001	<0,05	<0,001	<0,001
		Normothermia	134,2±0,9	63,2±8,3	72,8±5,6	75,2±5,7
	P_1			<0,001	<0,001	<0,001
A-VpO_2, mm Hg	P_2	Hypothermia	—	46,1±5,8	31,8±4,9	18,6±3,5
				<0,05	<0,001	<0,001
		Normothermia	—	71,0±7,9	61,4±5,0	59,0±5,1
pCO_2, mm Hg		Hypothermia	37,5±1,2	51,2±1,7	44,7±1,6	39,5±1,3
	P_1			<0,001	<0,001	>0,05
	P_2		<0,01	>0,05	<0,05	<0,01
		Normothermia	32,7±0,8	57,3±2,7	55,1±4,4	52,4±4,0
	P_1			<0,001	<0,001	<0,001
V-ApCO_2, mm Hg		Hypothermia	—	13,6±1,3	7,9±0,99	2,5±0,5
	P_2			<0,01	<0,01	<0,001
		Normothermia	—	24,6±2,9	22,4±4,5	19,7±4,2
pH		Hypothermia	7,50±0,04	7,37±0,04	7,362±0,04	7,371±0,04
	P_1			<0,05	<0,05	<0,05
	P_2		>0,05	>0,05	>0,05	>0,05
		Normothermia	7,529±0,04	7,301±0,06	7,295±0,06	7,314±0,05
	P_1			<0,05	<0,01	<0,01
Lactate, mg%		Hypothermia	—	7,85±0,83	4,9±0,78	3,16±0,54
	P_2			<0,01	<0,01	<0,01
		Normothermia	—	11,50±0,83	7,74±0,44	5,36±0,37
Pyruvate, mg%		Hypothermia	—	0,51±0,05	0,39±0,04	0,26±0,02
	P_2			>0,05	>0,05	>0,05
		Normothermia	—	0,36±0,08	0,30±0,06	0,26±0,06
Lactate/pyruvate		Hypothermia	—	16,23±2,27	12,91±2,06	9,74±1,92
	P_2		—	<0,05	<0,05	<0,05
		Normothermia	—	43,68±9,99	38,66±11,37	31,06±9,1
K^+, meq/liter		Hypothermia	3,56±0,19	3,56±0,12	3,74±0,14	3,71±0,15
	P_1			>0,05	>0,05	>0,05
	P_2			>0,05	>0,05	>0,05
		Normothermia	3,56±0,19	3,85±0,16	3,83±0,17	3,79±0,17
	P_1			>0,05	>0,05	>0,05
Na^+, meq/liter		Hypothermia	193,1±5,8	191,7±6,8	192,7±5,6	190,5±5,9
	P_1			>0,05	>0,05	>0,05
	P_2			>0,05	>0,05	>0,05
		Normothermia	193,1±5,8	188,4±8,9	189,2±9,2	190,1±9,5
	P_1			>0,05	>0,05	>0,05

Legend. P_1) Significance of differences between original and outflowing perfusion fluid after 1, 3, and 5 min; P_2) significance of differences between identical stages of normothermic and hypothermic series.

EXPERIMENTAL RESULTS

The experiments showed that pO_2 and A-VpO_2 in the outflowing fluid were reduced at all stages of perfusion in both series (Table 1). During hypothermia the decrease in A-VpO_2 was characteristically more marked. The increase in pCO_2 in the outflowing perfusion fluid, especially in the case of normothermic perfusion, was evidently due to elimination of CO_2 from the brain tissue. The dynamics of V-ApCO_2 during normothermic perfusion, unlike hypothermic, indicated constant and intensive uptake of CO_2 by the perfusion fluid.

Investigation of pO_2 and RP in the cerebral cortex showed that lethal exsanguination is accompanied by a fall in pO_2 (53.2 ± 5.3%; $P < 0.001$) and in RP (-21.1 ± 3.6 mV; $P < 0.001$). Compared with the final stage of exsanguination, after the 1st minute of hypothermic perfusion an increase in pO_2 was observed (78.0 ± 5.1%; $P < 0.01$), and after the 5th minute the value of pO_2 was 57.0 ± 5.3% ($P > 0.05$). In this series the fall in RP was even greater than after exsanguination, and by the 5th minute of perfusion it was −37.0 ± 3.4 mV ($P < 0.01$). During normothermic perfusion pO_2 increased after 1 min by a lesser degree (67.1 ± 3.9%; $P < 0.05$), and after 5 min it was 44.2 ± 3.4% ($P > 0.05$). RP remained at its level in the final stage of exsanguination. These results show that during hypothermic perfusion oxidation—reduction processes in the brain are inhibited.

In hypoxia, activation of anaerobic glycolysis is known to take place in brain tissue with the accumulation of lactate, in proportion to the severity of the hypoxic brain damage [3]. In the present experiments the hydrogen ion concentration (pH) fell in the outflowing perfusion fluid in both series and lactate and pyruvate appeared. This is evidence of their elimination from the brain and it also shows that regional craniocerebral perfusion cannot completely prevent hypoxic changes and activation of anaerobic glycolysis. Meanwhile the lower lactate concentration and the much lower lactate/pyruvate ratio in the outflowing fluid during hypothermic perfusion are evidence of considerable inhibition of anaerobiosis, possibly on account of cold inhibition of enzyme systems. During normothermic perfusion the minimal metabolic activity of the brain was somewhat prolonged.

Changes in the K^+ and Na^+ concentrations in the outflowing fluid in both series compared with the original solution were not significant; in our view this was due to the use of an extracellularly balanced perfusion fluid.

These experiments thus showed that under conditions of acute hypoxia, normothermic and, in particular, hypothermic intravascular perfusion of the brain with colloid–salt solution reduces the severity of disturbance of metabolic homeostasis.

LITERATURE CITED

1. V. L. Radushkevich, Infusion Therapy in Surgery [in Russian], Barnaul (1972), pp. 68-70.
2. V. L. Radushkevich, in: Abstracts of Proceedings of the 1st All-Russian Congress of Anesthesiologists and Reanimatologists [in Russian], Sverdlovsk (1974), pp. 488-490.
3. R. Kh. Tsupping, A. A. Tikk, and E. Yu. Kross, in: Neuropathology and Psychiatry [in Russian], Riga (1970), pp. 208-212.