EARLY POSTRESUSCITATION CENTRALIZATION OF THE CIRCULATION

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Reduction of the cardiac output and redistribution of the regional blood flow both play very important roles in the pathogenesis of circulatory disorders in shock and terminal states [3, 5, 11, 13]. However, the character of distribution of the cardiac output in the postresuscitation period is not yet clear in spite of data indicating the existence of differences in the pattern of the recovery of the blood flow in different organs [4, 6, 9].

In the investigation described below the distribution of the principal fractions of the cardiac output in the course of the early postresuscitation period was investigated.

EXPERIMENTAL METHOD

Experiments were carried out on 37 noninbred cats with an average weight of 3.20 ± 0.13 kg, anesthetized with pentobarbital (40-45 mg/kg, intraperitoneally), and heparinized (500-800 U/kg, intravenously). In the experiments of series I (n = 10) the cardiac output (CO) was studied by the thermodilution method [2] and the volume velocity of the blood flow in the thoracic part of the posterior vena cava was determined by the local thermodilution method. On the basis of the results the fraction of the cardiac output supplying the anterior (supradiaphragmatic) and posterior (subdiaphragmatic) parts of the body and also the coefficient of centralization of the circulation (CCC) were calculated. This coefficient is the ratio of the supradiaphragmatic fraction of CO to the total CO [5]. In the experiments of series II (n = 14) CO was studied by the thermodilution method, and the blood flow in the abdominal (subdiaphragmatic) part of the aorta was determined by means of an MF-27 electromagnetic flowmeter ("Nihon Kohden," Japan).* The blood flow in the supradiaphragmatic portion and CCC were calculated. Clinical death was induced in these series of experiments by arterial exsanguination and the animals were resuscitated by Negovskii's method without the use of adrenalin or other stimulants. In the experiments of series III, before arterial exsanguination, the animals (n = 13) were subjected to hemorrhagic hypotension (Wiggers' model, 6.67 kPa, or 50 mm Hg) for 30 min. The duration of clinical death in these experiments also was 5 min (the program of resuscitation measures also included indirect massage and defibrillation). In the course of the experiments the character of recovery of the vital functions was assessed by the usual tests. In animals in the experiments of series I and III the survival rate (observations continued for 10 days) and the neurologic deficit (according to a modified 100-point scale [14]) also were estimated.

EXPERIMENTAL RESULTS

Early parameters of restoration of vital functions in experiments of series I and II did not differ significantly. On average (M ± m) cardiac activity was restored after 39 ± 5 sec, respiration after 2.6 ± 0.4 min, and corneal reflexes after 18.4 ± 1.7 min. In animals in a terminal state complicated by preliminary hemorrhagic hypotension (series III), the corresponding values were 56 ± 7 sec and 8.2 ± 1.2 and 22.0 ± 2.9 min.

*These experiments were carried out in the Laboratory of Pathophysiology (Director, Dr. Med. Sci. G. S. Mazurkevich), N. I. Dzhanelidze Emergency Aid Research Institute, Leningrad.

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TABLE 1. CO, Its Fractions, and CCC in the Early Postresuscitation Period (M ± m)

Parameter	Series of expts.	Original data	Postresuscitation period, min				
			3	15	30	60	120
CO, ml/kg	I	161±10,0	241±14,6*	184±13,2**	161±16,8	137±12,7*	126±9,9*
	II	117±7,8	166±15,3*	123±7,6	107±6,2**	102±5,4*	81±4,0*
	III	190±9,2	230±24,3**	196±16,6	160±8,2*	154±13,0*	139±13,8*
Supradiaphragmatic fraction, ml/kg	I	78±4,4	137±9,6*	96±6,7*	80±9,8	67±7,9	57±5,9*
	II	54±5,9	107±12,0*	70±5,2**	55±4,4	50±3,4	37±2,4*
	III	87±5,2	150±18,4*	113±9,7*	89±8,3	68±7,6	59±6,6*
Subdiaphragmatic fraction, ml/kg	I	83±7,4	104±7,9**	88±9,7	81±9,7	70±7,1	69±7,1**
	II	63±4,4	59±7,6	53±4,4**	52±3,4**	52±3,7**	44±2,7*
	III	103±8,3	80±10,7**	83±12,2	71±4,3*	88±8,0	80±9,5**
CCC, conventional units	I	0,48±0,02	0,57±0,02*	0,52±0,02	0,50±0,04	0,49±0,03	0,45±0,04
	II	0,46±0,03	0,64±0,03*	0,56±0,02**	0,51±0,02	0,49±0,02	0,46±0,2
	III	0,46±0,03	0,65±0,04*	0,58±0,04*	0,55±0,03*	0,44±0,04	0,42±0,03

Legend. *P < 0.05 by Student's test, **P ≤ 0.05 by Wilcoxon's T test, compared with initial data.

Changes in CO in the postresuscitation period were typical and included a short hyperperfusion and subsequent hypoperfusion phases (Table 1). Significant differences were found in the time course of the principal flow rates in the initial stage. In the case of rapid death (series I) the anterior, supradiaphragmatic fraction of CO increased more than the subdiaphragmatic fraction. In animals in the experiments of series II, which did not differ in the severity of the actual terminal state, but underwent relatively greater trauma due to the experimental technique, no increase in blood flow was observed in the abdominal aorta. In animals in the terminal state complicated by hypotension, during the increase in CO its subdiaphragmatic fraction was significantly less than initially.

In the initial stage of the early postresuscitation period there is thus a redistribution of blood flows, as a result of which the blood supply to organs located in the supradiaphragmatic part (brain, heart, respiratory muscles, etc.) becomes much more rapid, i.e., the circulation is centralized. The intensity and duration of this reaction correlate directly with the severity of the terminal state endured.

The phenomenon of centralization of the circulation is well known in hypovolemic shock [3, 5, 11, 13]. The basic distinguishing feature of early postresuscitation centralization of the circulation is that it arises under normovolemic conditions and is evidently connected with the character of hypoxic (posthypoxic) lowering and recovery of vascular tone in different regions.

Redistribution of blood flows takes place in the course of resuscitation measures; the blood supply to the brain, moreover, is maintained at 90% of its initial level [15]. It is also known that administration of adrenalin potentiates this reaction even more during resuscitation [10]. Considering the experimental data, which demonstrate the importance of α-adrenergic stimulation for a favorable outcome of resuscitation [12], there are sufficient grounds for considering that centralization of the circulation is an adaptive reaction, contributing to the fastest possible restoration of the vital functions.

At the same time, excessive and prolonged centralization of the circulation in the early postresuscitation period may evidently have an unfavorable effect. Analysis of the end results of resuscitation in the experiments of series I and III showed that CCC increased more in animals which survived up to 24 h inclusive than in those which survived without any evident neurologic deficit. The maximal value of CCC in the period of hyperfunction was 0.69 ± 0.03 in the former and 0.60 ± 0.02 in the latter (P < 0.05).

On theoretical grounds, the unfavorable effect of excessive centralization of the circulation may be attributed to a sudden increase in blood supply to the brain. Severe hypoxia is known to abolish autoregulation of the cerebral circulation [7]. A considerable increase in volume perfusion under these conditions is naturally accompanied by an increase in the intravascular blood volume and pressure. It has been shown experimentally that in such a situation transcapillary metabolism is disturbed and cerebral edema develops [8]. Definite confirmation of the reality of these events in the postresuscitation period is given by the results of an investigation of impedance of the cerebral cortex [1]. In animals dying within

a few hours after clinical death from slow blood loss, a shift of fluid into the cellular sector took place in the initial stage of the postresuscitation period. This may perhaps be the reason why an increase in the cerebral flow in the early stages of the postresuscitation period due to administration of adrenergic drugs does not improve, but impairs the restoration of brain functions after long periods of clinical death [6]. Conversely, stabilization of arterial pressure and removal of the load from the venous system, by reducing the volume perfusion, help to produce some improvement in the course of recovery processes.

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EFFECT OF DOPAMINE AGONISTS AND ANTAGONISTS ON ENERGY RESOURCES OF THE RAT GASTRIC MUCOSA IN EXPERIMENTAL STRESS

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The writers showed previously [2, 3] that the antiulcerogenic action of metoclopramide is due to blocking of dopamine receptors in the CNS, which weakens the autonomic effect of stress-inducing stimulation, and not to the ability of metoclopramide to stimulate gastric and intestinal movement, as was hitherto considered [7]. This conclusion was based on an evaluation of the vulnerability of the gastric mucosa to attack by stress-inducing factors after preliminary administration of dopamine agonists and antagonists to animals. It was interesting to discover how the energy resources of the gastric mucosa change under these circumstances, in the light of Menguy's hypothesis [8, 11] that in stress induced by massive

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