EXPERIMENTAL USE OF EXTRACORPOREAL HEMADSORPTION IN THE POSTRESUSCITATION PERIOD

V. A. Negovskii,* I. O. Zaks, and V. M. Shapiro

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For detoxication purposes in the early postresuscitation period hemadsorption on activated charcoal was used. Hemadsorption in dogs resuscitated after circulatory arrest for 15 min as a result of electric shock led to earlier recovery of the corneal reflexes and significantly improved the outcome of resuscitation both by removal of incompletely oxidized metabolic products and also, perhaps, removal of other toxic products.

KEY WORDS: hemadsorption; postresuscitation period.

In the postresuscitation period, besides the restoration of functions, new pathological changes may arise and aggravate those established as a result of the primary hypoxia [7], with the development of "resuscitation sickness." An important role in the pathogenesis of this disease is played by postresuscitation toxemia. The nature of the toxins causing the toxemia has not yet been finally settled. The range of toxic factors evidently includes incompletely oxidized metabolic products, bacterial toxins penetrating from the intestine, and biologically active substances. The more rapidly and completely the pathogenic influence of extracerebral factors acting in the early resuscitation period on the brain can be reduced to a minimum, the greater the chance of a complete recovery. Several different methods of detoxication, including blood replacement, plasmapheresis, donor circulation, have a favorable effect on the course of the recovery period and the outcome of resuscitation [1, 2, 8].

The use of activated charcoal as an adsorbent of toxic products is known to give good results in the treatment of hepatic and renal failure [3, 4, 11] and in the treatment of exogenous poisoning [4, 5, 12].

The object of the present investigation was an experimental study of the effect of hemadsorption, carried out at the beginning of the recovery period after circulatory arrest for 15 min, caused by electric shock, on the outcome of resuscitation and on some indices of metabolism.

EXPERIMENTAL METHOD

Experiments were carried out on dogs weighing 10-14 kg. Omnopon (6-8 mg/kg) premedication was given. The vessels were dissected under local anesthesia in conjunction with superficial pentobarbital anesthesia (3-4 mg/kg). Heparin (300 mg/kg) was injected. Circulatory arrest caused by electric shock continued for 15 min. Resuscitation was carried out by the method developed in the Laboratory of General Resuscitation, Academy of Medical Sciences of the USSR [6].

In the experiments of group 1 (six dogs) hemadsorption was begun after the resumption of cardiac activity at the 4th-5th minute of resuscitation, by perfusing the blood through an arteriovenous shunt with an adsorption column. A roller pump (output 40-50 ml/min, capacity of column 275 ml) was used for perfusion. IGI No. 5 charcoal, pH 9.1-9.2, was used as the adsorbent. Since the columns were filled with physiological saline, simultaneously with the beginning of perfusion, injection of 10% albumin solution (7-10 mg/kg) began in order to prevent the development of edema, for albumin possesses water-binding properties. The duration of hemoperfusion was 30 min. After the end of hemoperfusion the blood filling the column was slowly injected into a vein under control.

*Academician of the Academy of Medical Sciences of the USSR.

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TABLE 1. Changes in Indices Studied during Passage of Blood through Perfusion Column

Time of hemadsorption, min	Δ pH	ΔBE, meq/liter	Δ lactate, mg%	Δ protein, %
5	+0,48±0,01	+7,2±0,9	−36,0±3,4	−1,03±0,2
25	+0,28±0,01	+7,1±1,1	−17,1±2,8	−0,40±0,1

TABLE 2. Dynamics of Indices of Acid-Base Balance in Postresuscitation Period in Animals of Groups 1 and 2

Time of sampling	Group 1				Group 2			
	pH	BE, meq/liter	lactate, mg%	protein, %	pH	BE, meq/liter	lactate, mg%	protein, %
30 min	7,13±0,01	−16,8±0,7	72,0±3,7	5,47±0,4	7,06±0,01	−20,1±0,9	74,3±4,9	5,61±0,3
1 h	7,19±0,01	−15,1±0,6	39,6±4,5	—	7,15±0,01	−17,6±0,5	41,8±3,9	—
3 h	7,25±0,02	−9,0±0,7	20,7±2,7	—	7,22±0,01	−13,7±0,8	23,0±1,8	—

In the experiments of group 2 (control, five dogs) physiological saline and albumin were injected intravenously after the resumption of cardiac activity in the same doses as in the experiments of group 1; no hemadsorption was carried out.

Hemadsorption also was carried out on three healthy dogs.

In the initial state, at the 3rd to the 4th minute of resuscitation, and 10 min (after 5 min of hemadsorption), 30 min (25 min of hemadsorption), and 1 and 3 h of resuscitation samples of arterial blood were taken. The samples were taken from blood entering and leaving the column. Indices of the acid-base balance were determined with the micro-Astrup apparatus, lactic acid was determined by an enzymic method, and the protein concentration refractometrically.

EXPERIMENTAL RESULTS AND DISCUSSION

The performance of hemadsorption on healthy animals had no marked effect on the hemodynamics or on the indices of the acid-base balance. The arterial blood pressure (BP) was virtually unchanged. In the process of adsorption the pH of the blood at the outlet from the column rose sharply (to 7.80 ± 0.03 after 5 min of adsorption and to 7.68 ± 0.02 after 25 min), the base deficit was reduced (by 5-7 meq/liter), and the blood protein concentration fell (by 1-1.5%). A considerable fall in pCO_2 and pO_2 was observed. However, no changes were observed in the blood stream: Throughout the period of hemadsorption the indices studied remained at their initial level. The compensatory powers of the healthy body are evidently sufficient to maintain homeostasis. Similar results were obtained by Barakat and MacPhee [10]. The dogs were to all intents and purposes healthy on the day after the experiment.

In animals surviving clinical death hemadsorption was started in the initial period of resuscitation, when the incompletely oxidized metabolic products accumulating in the tissues begin to enter the blood stream and a sharp acidotic shift is observed, the pH of the blood falls to 7.0 or below, and the lactic acid concentration rises to 72.1 ± 9.0 mg%. The toxicity of the blood during the first 30 min of the postresuscitation period rises sharply [9].

Connection to the column facilitated the adsorption of acid metabolic products (Table 1).

During adsorption the pH of the blood at the outlet from the column rose above its initial values (7.45 ± 0.02 at the 5th minute). This increase in pH evidently took place both on account of loss of acid metabolites (36.0 ± 3.4 mg% of lactic acid was deposited on the sorbent at the beginning of adsorption, and the base deficit fell to 13.5 ± 0.7 meq/liter), and on account of loss of carbon dioxide – the pCO_2 of the blood fell below 10 mm Hg. Meanwhile oxygen also was adsorbed and pO_2 fell to 30 ± 12 mm Hg. However, since the blood passed from the column into a vein of the pulmonary circulation, the loss of O_2 was unimportant.

Despite injection of albumin, the deposition of protein on the sorbent had the result that in the initial period of resuscitation there was a protein deficiency compared with the experiments of group 2 (4.09 ± 0.3 and 5.48 ± 0.4% in groups 1 and 2 respectively). By the 30th minute of the postresuscitation period the protein concentration in the blood did not differ significantly from the initial values.

Active removal of acid metabolites from the blood, incidentally, resulted in the acidotic shift of the blood in the experiments of group 1 during the first 30 min of the postresuscitation period to be less marked (Table

2). The differences in pH and BE were statistically significant ($P < 0.05$). However, toward the end of the 1st hour of resuscitation these differences disappeared. In the experiments of group 1 the rate of transfer of incompletely oxidized products from the tissues into the blood stream evidently increased, because of the concentration gradient at the tissue-blood boundary. During adsorption of uric acid after CCl_4 poisoning, no change in its concentration in the blood stream likewise was observed [3].

The values of pH and BE 3 h after resuscitation in the experiments of group 1 did not differ significantly from their initial levels, whereas in the experiments of group 2 they were a little lower still than their initial level.

Hemadsorption aggravated the instability of BP which is usually found in the early postresuscitation period. Immediately after connection of the column BP began to fall, and despite repeated injections of adrenalin and ephedrine, it was very difficult to keep it above the critical level, which is particularly important in resuscitation practice. This may be connected with loss of glucocorticoids [8], extracted with the protein molecules, on the sorbent. Potassium also was lost from the blood plasma (to 1 meq/liter).

Despite this complication, however, earlier recovery of the corneal reflexes (18 ± 0.4 and 23 ± 0.3 min in groups 1 and 2 respectively) was observed in the animals of group 1. All six animals on whom hemadsorption was carried out in the early recovery period survived. Complete recovery of the functions of the CNS, judging from the external appearance and behavior of the animals, took place in five cases, and hearing and sight were restored on the 1st-2nd day. Disturbances of static posture continued in one dog for a long time (up to 3 weeks). Of the five animals of group 2, complete recovery of the functions of the CNS was found in only two. The rest died on the 1st or 2nd days after the experiment.

Hemadsorption in the early postresuscitation period is thus an efficient method of detoxication. It enabled the acidotic shift in the blood to be corrected in the first 30 min of the resuscitation period, led to the earlier recovery of the corneal reflexes, and considerably improved the results of resuscitation, possibly through the removal of other toxic products also.

Although the data described in this paper are preliminary in character, it can nevertheless be concluded from them that hemadsorption is a promising method for the control of toxemia during resuscitation, one of the most important pathogenetic factors in postresuscitation sickness.

A key question which largely determines the prospects for the use of hemadsorption in resuscitation at the present time is the availability of sorbents capable of selectively eliminating from the circulation toxins specific for terminal states, yet at the same time having a less harmful action on the internal media of the body (on the blood cells, proteins, hormones, and so on). It will be obvious that the problems facing experimental resuscitation are much more difficult than the problems arising in connection with the use of hemadsorption in toxicology, where the investigator is dealing with one particular toxin with clearly defined properties. Unfortunately the range of sorbents currently available is extremely limited, and they do not possess all the necessary properties. The search for new active substances is an urgent task.

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