PHYSIOLOGICAL ASSESSMENT OF AUTOHEMOPERFUSION THROUGH ACTIVATED CHARCOAL

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The adsorptive properties of phenolformaldehyde-activated charcoal with respect to physiologically active substances were studied after static conditions (adsorption from physiological saline) and during autohemoperfusion of the limb vessels at constant rate in experimental animals. Phenolformaldehyde-activated charcoal was found to adsorb serotonin, adrenalin, noradrenalin actively and histamine to a lesser degree from physiological saline. Activated charcoal readily adsorbed serotonin, adrenalin, noradrenalin, and acetylcholine, histamine less readily, and papaverine only very slightly from flowing blood. When the column of charcoal adsorbent was connected to a main vessel of the animal no changes were observed in the systemic blood pressure, but in some cases the perfusion pressure fell on account of a decrease in the resistance of the vessels studied.

KEY WORDS: adsorption blood purification; hemoperfusion; activated charcoal; physiologically active substances

Reports of the use of activated charcoal for the adsorption purification of blood in the treatment of acute poisoning [1, 15], hepatic failure [6, 11, 14], and renal failure [10, 12, 16] have recently been published. Hemoperfusion through a column containing activated charcoal was shown to change certain physiological parameters: It reduced the arterial and venous blood pressure and changed the respiration and pulse rates [1, 6, 14, 17].

These observations suggest that, besides removing toxins from the body, activated charcoal also adsorbs endogenous physiologically active substances concerned with the maintenance of normal homeostasis from the blood stream.

The object of this investigation was to verify this hypothesis and to study the adsorbent properties of phenolformaldehyde-activated charcoal (PFAC) in relation to certain physiologically active substances.

EXPERIMENTAL METHOD

PFAC is a coarse-mesh charcoal with an ash content of under 0.05% and was synthesized by carbonization of phenolformaldehyde resin and subsequent activation of the crude charcoal at 950-1000°C in an atmosphere of carbon dioxide to 50% combustion loss. The charcoal was prepared as smooth, irregularly shaped granules measuring 0.5-1.0 mm and possessing high surface strengths.

The experiments of series I to study adsorption of physiologically active substances under static conditions were carried out at 20°C by the usual method [8]. The concentrations of the initial solutions of adrenalin, noradrenalin, serotonin, and histamine in physiological saline varied from $1 \cdot 10^{-4}$ to $1 \cdot 10^{-3}$ M. The corresponding solutions (20 ml) were poured on weighed samples (0.1 g) of charcoal. After incubation for 3 h with constant stirring the solutions were separated from the adsorbents and equilibrium concentrations of the dissolved substances were determined on a spectrophotometer (Specord VIS) at the following wavelengths (in nm): serotonin 275, histamine 212, adrenalin and noradrenalin 280. The degree of absorption was expressed in grams adsorbate per gram adsorbents.

The experiments of series II to study adsorption of physiologically active substances under dynamic conditions were carried out on dogs anesthetized with morphine and chloralose, and by the use of a technique of resistography [9] based on orthohemoperfusion of the blood vessels to be studied (in the hind limb) by means of a constant delivery pump.

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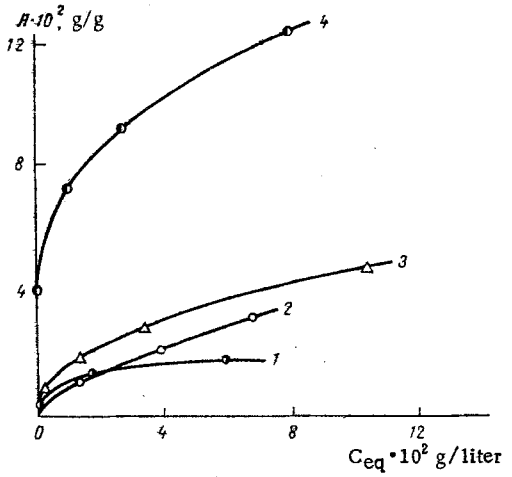

Fig. 1. Isotherms of adsorption of histamine (1), adrenalin (2), noradrenalin (3), and serotonin (4) from physiological saline on phenolformaldehyde-activated charcoal at 20°C. Abscissa, amount of adsorption (in g adsorbate/g adsorbent); ordinate, equilibrium concentrations of solutions of test substances (in g/liter solution).

TABLE 1. Magnitudes of Responses (in mm Hg) of Vessels of Dog Hind Limb to Vasoactive Substances when Injected into Regional Blood Flow through By-Passed Vessel (I) and through Column with Activated Charcoal (II)

Statistical index	Adrenalin		Nonadrenalin		Acetylcholine		Histamine		Serotonin		Papaverine	
	I	II	I	II	I	II	I	II	I	II	I	II
M	+29	+3	+24	+3	−35	−3	−35	−10	−32	−3	−31	−21
$\pm m$	±4,23	±0,2	±2,95	±0,73	±2,17	±1,05	±3,98	±2,92	±3,74	±1,19	±4,34	±2,93
P	<0,001		<0,001		<0,001		<0,001		<0,001		<0,05	
n	37		37		29		20		14		22	

The column containing PFAC and, parallel with this, the by-passed main vessel (the volume of the shunt was equal to the volume of the intergranular space in the column containing the adsorbent) were arranged along the input line of the perfusion pump. Before operation, the column containing 70 ml of absorbent, bounded on both sides by gauze filters, was primed with physiological saline containing heparin (500 i.u.).

The systemic arterial pressure and the perfusion pressure in the limb vessels were recorded by electromanometers as blood flowed through the bypass and through the adsorbent. In both cases the responses of the limb vessels were recorded during injection of vasoactive substances into the perfusion system (adrenalin 0.001-0.004 mg, noradrenalin 0.001-0.004 mg, serotonin 0.2-1.0 mg, histamine 0.01-0.02 mg, acetylcholine 0.05-0.20 mg, and papaverine 0.4-0.8 mg). The recordings were made on the USCh-8 automatic ink recorder.

The adsorption properties of PFAC were judged by comparing the magnitudes of the vascular responses to injection of equal doses of the vasoactive substances into the by-passed vessel and into the vessel connected to the adsorbent.

EXPERIMENTAL RESULTS AND DISCUSSION

The results of the study of adsorption of the substances from physiological saline are given in Fig. 1. They show that, within the region of equilibrium concentrations tested, charcoal has high adsorbent affinity for compounds of this type. The character of the adsorption isotherms for serotonin, adrenalin, and noradrenalin (a rise of the isotherm in the region of fairly high equilibrium concentrations and the absence of a plateau) suggests that these substances ought to be adsorbed by charcoal in large quantities also when present in solution in higher concentration, for the shape of the isotherm of adsorption of histamine from physiological saline points to the more rapid saturation of the adsorbent by this substance.

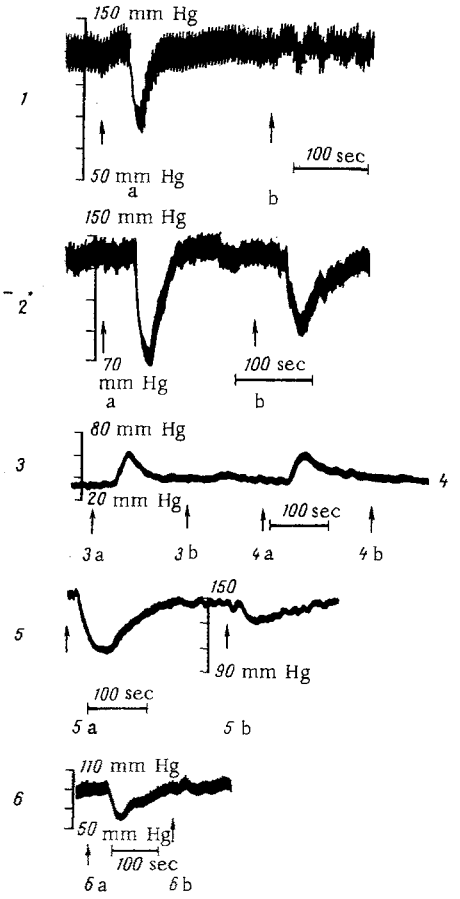

Fig. 2. Vascular responses to injection of acetylcholine (1), papaverine (2), adrenalin (3), noradrenalin (4), histamine (5), and serotonin (6) into by-passing main vessel (a) and into vessel before column with activated charcoal (b). Arrows below curve of perfusion pressure denote times of injection of vasoactive substances.

In 30 experiments with autohemoperfusion the adsorbent was in contact with blood on average for 1.5 h. When hemoperfusion was carried out through activated charcoal, no changes in the systemic arterial pressure were observed in response to inclusion of the adsorbent in the blood flow. The level of the perfusion pressure in the limb vessels when the column with adsorbent was included in the perfusion system was unchanged in 40% of the experiments, and reduced in the rest, down to a mean value of 79% of the initial level ($P < 0.001$). In these cases before the vascular responses were reproduced the perfusion pressure was artificially stabilized by increasing the output of the pump. The results (Table 1) are evidence of the high adsorbent properties of PFAC and they correlate closely with the results of adsorption from physiological saline. For instance, the responses to adrenalin, noradrenalin, acetylcholine, and serotonin virtually disappeared when these substances were injected at the entry to the column containing the adsorbent, the response to histamine was reduced on average by 26% ($P < 0.001$), whereas the response of the perfused vessels to papaverine was reduced by 8.5%.

Resistograms illustrating the above findings are given in Fig. 2. One possible explanation of the observed fall in the level of the peripheral vascular resistance during perfusion through activated charcoal may be that pressor amines, which in some cases may participate in the formation of the initial vascular tone, are adsorbed from the circulating blood. There are no data in the literature to confirm that physiological blood concentrations of catecholamines in the resting state may exert a constant pressor effect on the smooth muscle of the vessels [3, 13]. However, in stress situations the blood concentration of the hormonal components of the sympathico-adrenal system may exert their action on the heart and vessels [2, 4, 13]. Probably differences in the depth of anesthesia and severity of the operative trauma in some experiments caused an increase in the blood concentration of catecholamines, with the result that they participated in the formation of the initial level of resistance to the blood flow. It is in these cases that adsorption of adrenalin and noradrenalin from the flowing blood could cause a decrease in the resistance of the perfused limb vessels. This suggestion is in agreement

with the view of Levtov and Parolla [5] that the role of the blood catecholamines in the maintenance of vascular tone in the limb is inconstant.

The data on the adsorbent properties of activated charcoal relative to the physiologically active substances of the blood thus obtained can be used to study the causes of changes in certain physiological parameters during hemoperfusion through activated charcoal.

From the technical point of view it is important to note that connecting a column with charcoal hemadsorbent to the main artery leads to partial humoral isolation of the test organ. If blood flowing along the main vein is also passed through a column with hemadsorbent, it becomes possible to study the peripheral and central components of the response of the cardiovascular system to injection of physiologically active substances separately. This considerably broadens the experimental field in this region, more especially because, instead of activated charcoal, selective adsorbents synthesized specially for the removal of a particular compound from the blood stream can be used.

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