EFFECT OF ADRENERGIC BLOCKADE ON AUTOREGULATION OF THE CEREBRAL BLOOD FLOW DURING ORTHOSTATIC TESTS

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UDC 612.824.014.46:615.217.24

In experiments on rats under local anesthesia the action of phentolamine and propranolol on autoregulation of the cerebral blood flow (ACB) was studied during orthostatic tests (OT). The cerebral blood flow was measured in the carotid system, the venous pressure in the cerebral vessels, and the perfusion pressure in the carotid arteries; the resistance of the cerebral vessels was calculated. OT were simulated by tilting a special table with the animal (head upward or downward) through 40-80° from the horizontal plane. The results showed that adrenergic blockade in most cases of OT disturbed ACB: phentolamine led to a passive increase in the cerebral blood flow in response to an increase in perfusion pressure, whereas propranolol, on the other hand, caused a passive decrease in the cerebral blood flow in response to a fall of perfusion pressure.

KEY WORDS: cerebral circulation; adrenoblockers; autoregulation.

Orthostatic hypotension arising during treatment with antiadrenergic drugs is frequently accompanied by disturbance of the cerebral circulation and by loss of consciousness. The insufficiency of the cerebral blood flow in these cases may arise through disturbances of autoregulatory mechanisms, but the influence of adrenergic blockade on autoregulation of the cerebral circulation has not been adequately studied [10, 11, 12], and for that reason it was decided to undertake the present investigation.

EXPERIMENTAL METHOD

Experiments were carried out on 25 rabbits weighing 2.5-3.5 kg. The unanesthetized animals were fixed to a special table whose position in the vertical plane could be changed. The cerebral blood flow was recorded by means of a flowmeter of the writers' own design [2] in the common carotid arteries, the extracranial branches of which were ligated. The blood pressure (BP) was recorded by means of a mercury manometer in the common carotid artery. The pressure in the venous system of the brain was measured with a water manometer connected to the cranial end of the external jugular vein or sagittal sinus. Heparin was used as anticoagulant. All operations connected with dissection, ligation, and cannulation of the vessels were carried out under local procaine anesthesia. This anesthesia evidently also blocked nervous reflex control of the carotid sinuses, so that more lasting changes in BP were produced during orthostatic tests (OT) [3, 9].

OT lasting 3-5 min were simulated by turning the table with the animal (head upward or downward) through 40-80° from the horizontal plane. Under similar conditions, Moskalenko and co-workers [5, 6] observed certain changes in the dynamics of the blood volume of the brain.

In each experiment several OT were performed before (control) and after administration of the adrenolytics. α-Adrenergic receptors were blocked by phentolamine [1-3 mg/kg) and β-adrenergic receptors by propranolol (1-2 mg/kg). The antiadrenergic drugs were injected intravenously or intra-arterially (into the perfusion system of the flowmeter by means of a microinfuser). The character of changes in autoregulation of the cerebral blood flow (ACB) during OT was judged from changes in the indices of the cerebral blood flow, perfusion pressure, and resistance of the cerebral vessels. The perfusion pressure was calculated as the difference between the venous pressure and BP. The experimental results were subjected to statistical analysis by the direct differences method.

Department of Pharmacology, Pyatigorsk Pharmaceutical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 86, No. 9, pp. 309-311, September, 1978. Original article submitted March 22, 1978.

0007-4888/78/8609-1177$07.50

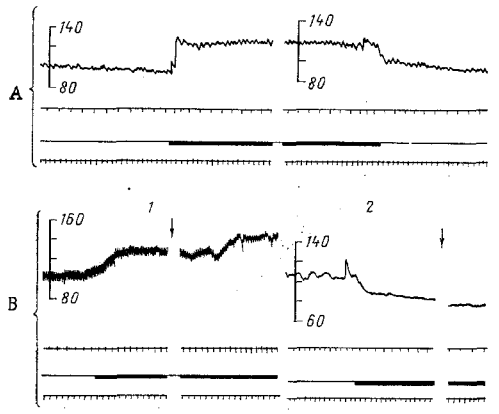

Fig. 1

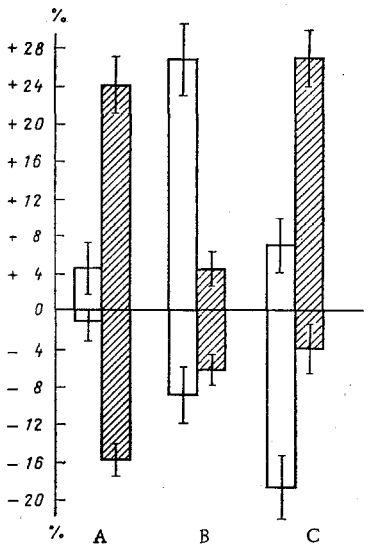

Fig. 2

Fig. 1. Cerebral blood flow during orthostatic tests before (A) and after (B) adrenergic block by phentolamine (1B) and propranolol (2B). From top to bottom: arterial blood pressure, cerebral blood flow (distance between markers 3.5 ml in A and 2 ml in B), orthostatic test, time marker (5 sec). Arrows indicate interruption of 1 min.

Fig. 2. Cerebral blood flow (unshaded column) and cerebral vascular resistance (shaded column) during orthostatic tests: head downward (above the line), head upward (below the line). A) Control, B) after phentolamine, C) after propranolol.

TABLE 1. Changes in Cerebral Blood Flow (CBF) and Cerebral Vascular Resistance (CVR) in Control and after Adrenergic Blockade (in % of initial data)

	Number of OT	Increase of perfusion pressure between 60 and 120 mm Hg		Number of OT	Decrease of perfusion pressure between 120 and 60 mm Hg	
		CBF	CVR		CBF	CVR
Control	30	+4,59±2,7	+24,0±3,0	35	−1,36±2,0	−16,08±1,7
P		>0,05	<0,001		>0,05	<0,001
After phentolamine	19	+27,6±3,8	+4,3±1,8	12	−9,03±3,0	−6,4±1,5
P		<0,001	<0,05		<0,05	<0,001
After propranolol	15	+6,9±2,8	+26,3±3,0	16	−18,8±3,3	−4,1±2,5
P		<0,05	<0,001		<0,001	>0,05

EXPERIMENTAL RESULTS AND DISCUSSION

With the animals in the horizontal position, the initial BP averaged 97.5 ± 3.9 mm Hg, the venous pressure 83.6 ± 5.0 mm water, and the resistance of the cerebral vessels 1.08 ± 0.06 mm Hg/100 g·min/ml. When the angle of tilting of the table was changed, with the animal's head above or below the horizontal plane, in most experiments stepwise changes in BP were observed within limits of 60-140 mm Hg, or in some cases, 40-160 mm Hg. The venous pressure varied between 20 and 170 mm water, and only rarely did it rise to 190 mm water or fall to zero. In 5 of the 25 rabbits changes in BP during OT were slight in degree and transient, or autoregulation was virtually absent. Only those experiments in which most OT before administration of the adrenolytics were accompanied by an autoregulatory response and by lasting changes in BP within the range from 60 to 120 mm Hg were therefore included in the data for analysis.

The increase in perfusion pressure during tilting of the animal with its head downward was accompanied by an increase in the resistance of the cerebral vessels by 24 ± 3% ($P < 0.001$) and in the cerebral blood flow by 4.6 ± 2.7% ($P > 0.05$). With a decrease in perfusion pressure (the animal tilted with its head upward), the cerebral vascular resistance decreased by 16.08 ± 1.7% ($P < 0.001$) and the cerebral blood flow by 1.36 ± 2.04% ($P > 0.05$). In control observations changes in perfusion pressure between 60 and 120 mm Hg were thus accompanied in most cases by an autoregulatory response of the cerebral vessels aimed at maintaining a comparatively stable cerebral blood flow (Fig. 1A and 2A). In some cases the cerebral blood flow showed a tendency toward passive changes depending on the perfusion pressure, evidence of insufficiency of ACB. In

other cases the cerebral blood flow decreased with a rise in perfusion pressure, and vice versa. This indicates excessive autoregulation, which is evidently the cause of spasm of the cerebral vessels during hypertensive crises.

Adrenergic blockade led to significant changes in ACB (Table 1; Fig. 1B). For instance, after blockade of the α-adrenergic receptors the increase in perfusion pressure during OT in animals with the head downward was accompanied by an increase in the cerebral blood flow and vascular resistance. With a decrease in perfusion pressure during OT (with the head upward), the cerebral vascular resistance and blood flow decreased. Consequently, blockade of the α-adrenergic receptors by phentolamine virtually abolished the autoregulatory vasoconstriction and weakened the vasodilatation to some extent (Fig. 2B). Weakening of the latter evidently facilitates the onset of orthostatic collapse, characteristic of α-adrenergic blockade.

During β-adrenergic blockade an increase in perfusion pressure was accompanied by an increase in the cerebral vascular resistance and blood flow. A decrease in perfusion pressure under these conditions caused a decrease in the cerebral blood flow and vascular resistance (Table 1), i.e., in most cases there was a passive decrease in cerebral blood flow corresponding to the decrease in perfusion pressure (Fig. 2C).

The results of this investigation thus showed that adrenergic blockade causes considerable changes in ACB during OT. These data are in agreement with modern views on the role of the sympathico-adrenal system in the regulation of the cerebral blood flow [1, 4, 12]. Assuming the nervous reflex genesis of these reactions [7, 8], the possibility cannot, however, be ruled out that local (metabolic and myogenic) mechanisms of regulation of cerebrovascular tone may also participate. The problem of relations between nervous reflex and local mechanisms and their interconnection still awaits elucidation.

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