CHANGES IN THE LOCAL CEREBRAL BLOOD FLOW ACCOMPANYING ELEVATION OF THE SYSTEMIC ARTERIAL PRESSURE IN ANIMALS

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The systemic arterial pressure was raised in normal rabbits and in rabbits with experimental renal hypertension by intravenous injection of noradrenalin and the local cerebral blood flow was recorded at two points of the cortex or white matter of the cerebral hemispheres by the hydrogen-clearance method, and the EEG also was recorded. A series of successive changes in the local cerebral blood flow was observed and these changes could be similar or different in duration and character at different electrodes. Pathological forms of activity were revealed on the EEG.

KEY WORDS: cerebral blood flow; hypertension.

The study of the cerebral hemodynamics by quantitative methods of determination of the local blood flow in animals with acute arterial hypertension and in patients during hypertensive crises is of recent origin [2-4, 7, 13, 14]. During elevation of the arterial blood pressure (BP) by intravenous injection of hypertensive substances or by compression of the aorta, the mechanisms of autoregulation may collapse and the cerebral blood flow increase. It has been assumed that in such cases the changes in the cerebral blood flow during elevation of AP were similar for the whole brain. However, injury to the brain tissue in hypertensive encephalopathy or in acute experimental arterial hypertension is known to be local or "mosaic" in character.

The object of the present investigation was to determine variations in the local cerebral blood flow (LCBF) in different parts of the brain of the same animal during acute arterial hypertension.

EXPERIMENTAL METHOD

Experiments were carried out on 12 normal rabbits and 22 rabbits with experimental renal hypertension caused by constricting both renal arteries for 2-8 months before the experiments (BP 120-190 mm Hg). The animals weighed 2.8-3.5 kg. Experiments were carried out under urethane anesthesia (1 g/kg) under normocapnic conditions (mean pCO_2 of the arterial blood 37 mm Hg) and slight compensated acidosis (mean pH of the arterial blood 7.38), both determined with the micro-Astrup apparatus. To determine LCBF (in ml/100 g tissue/min) by the hydrogen-clearance method [6], platinum electrodes were implanted into each rabbit into both hemispheres, mainly in zones on the boundary between territories supplied by branches of the anterior and middle cerebral arteries, 8-10 days before the experiments. An experimental "hypertensive crisis" was produced by intravenous injection of 10 ml of 0.02% noradrenalin solution in the course of 1.5-2 min. This raised BP in the course of 20-25 sec by 50-120 mm Hg, after which it remained high for 5-10 min. The noradrenalin concentration in the arterial blood determined by Matlina's fluorometric method reached 450-750 µg/liter

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TABLE 1. Type I Response of LCBF to Arterial Hypertension

No.	Initial value of LCBF (in ml/100 g/min)	LCBF (in ml/100 g/min)	
		2 min after beginning of noradrenalin injection	6-8 min after beginning of noradrenalin injection
1°	32	36	33
2°	38	37	Unchanged
3°	70	69	74
4°	52	59	62
5°	65	Unchanged	60
6+	46	46	46
7+	69	69	69
8+	69	63	60
9+	54	Unchanged	54
	$M_1=55\pm6$	$M_2=55\pm6$	$M_3=57\pm6$

$P_{M_1-M_2}>0{,}05$. $P_{M_2-M_3}>0{,}05$. $P_{M_1-M_3}>0{,}05$.

Legend. Here and in Tables 2 and 3: °) normal animals; +) animals with experimental renal hypertension.

TABLE 2. Type II Response of LCBF to Arterial Hypertension

No.	Initial value of LCBF (in ml/100 g/min	LCBF (in ml/100 g/min	
		2 min after beginning of noradrenalin injection	6-8 min after beginning of noradrenalin injection
10°	45	Increased	43
11°	75	128	75
12°	65	Increased	60
13°	47	138	47
14°	130	Increased	130
15+	46	85	46
16+	35	132	44
17+	53	135	58
18+	70	134	102
19+	39	62	31
	$M_1=63\pm6$	$M_2=116\pm12$	$M_3=66\pm7$

$P_{M_1-M_2}<0{,}02$. $P_{M_2-M_3}<0{,}02$. $P_{M_1-M_3}>0{,}05$.

TABLE 3. Type III Response of LCBF to Arterial Hypertension

No.	Initial value of LCBF (in ml/100 g/min)	LDBF (in ml/100 g/min)	
		2 min after beginning of noradrenalin injection	6-8 min after beginning of noradrenalin injection
20+	24	37	12
21+	40	Increased	21
22+	139	»	66
23+	140	260	62
24+	65	128	27
	$M_1=82\pm8$	$M_2=142\pm14$	$M_3=38\pm4$
	$P_{M_1-M_2}<0{,}02$. $P_{M_2-M_3}<0{,}01$. $P_{M_1-M_3}<0{,}02$.		
25+	33	23	12
26+	83	53	Rabbit killed
27+	76	51	"
28+	151	92	"
29+	140	103	"
30+	75	64	"
31+	65	36	"
	$M_1=89\pm9$	$M_2=60\pm6$	
	$P_{M_1-M_2}<0{,}02$		

plasma from an initial value of 23 μg/liter plasma, and it was comparable with the blood noradrenalin level of patients during hypertensive crises [1].

During the acute experiment BP was recorded continuously in the femoral artery. Simultaneously the value of pO_2 in the brain tissue was recorded polarographically, as an indicator of qualitative changes in the LCBF velocity [5, 10]. Immediately before the injection of noradrenalin and also 2 and 6-8 min after the beginning of the injection, the LCBF was recorded quantitatively by the hydrogen-clearance method. The state of the brain electrical activity was deduced from a study of the EEG and the corticogram. The animals were decapitated after the experiments and the ordinary histological investigation carried out. Characteristic changes of hypertension were found in the blood vessels of the brain and internal organs of the experimental animals. The electrode tips were located in the cortex or white matter of the parietal region.

EXPERIMENTAL RESULTS

Of the three types of changes in LCBF in response to acute arterial hypertension [4], the type I response (no change in LCBF; Table 1) and the type II response (an increase in LCBF as a result of temporary collapse of autoregulation of LCBF followed by its return to the initial level; Table 2) were found equally frequently in the normal animals and in animals with experimental renal hypertension. The type III response an increase in LCBF followed by a sharp and irreversible decrease, was recorded only in animals with experimental renal hypertension. The phase of increased blood flow was often of such short duration that the LCBF, recorded in the second minute, was below its initial level by a statistically significant degree (Table 3).

Despite the symmetrical implantation of the electrodes, different types of response of

LCBF to an equal rise of arterial blood pressure in the regions of insertion of the electrodes could be observed. In normal animals these were responses of types I and II, but in animals with experimental renal hypertension, different types of responses of LCBF were found more often and in widely different combinations. Even when the changes in LCBF were of the same type (II-II or III-III) the increase or decrease in LCBF by the second minute after injection of noradrenalin at one of the electrodes could be greater than at the other. As a rule more marked changes were recorded in the white matter (an increase of up to 400% and a decrease down to 45%), compared with only 200% and 60% in the gray matter. The reason for this difference was evidently the less active functioning of the autoregulation mechanism of LCBF in the white matter than in the gray [12].

The fact that the effect of the injected noradrenalin on the collapse of autoregulation of LCBF is mediated through the BP has been noted in the literature and was demonstrated by the writers in an additional series of experiments on 6 normal animals and 4 animals with experimental renal hypertension, into which noradrenalin was injected with the use of a BP compensator. The maximal changes in BP amounted to 20 mm Hg and no change in LCBF was recorded at any of the electrodes (i.e., a response of I-I).

With the collapse of autoregulation of the cerebral blood flow changes characteristic of a hypoxic state of the brain tissue were observed on the EEG for electrocorticogram. They were expressed as the appearance of pathological forms of electrical activity, and strengthening of the slow δ waves. Disturbances of electrical activity became more distinct toward 2-2.5 min on account of an increase in their amplitude. High-amplitude slow waves could be separated by small groups of pointed waves and spikes.

It has now been shown that acute arterial hypertension gives rise to local changes in permeability of the blood–brain barrier for proteins, and that these changes differ qualitatively and quantitatively in different parts of the brain [8, 9, 11]. Dissimilar changes in LCBF in the region of the different electrodes evidently reflect a locally developing collapse of autoregulation of the cerebral blood flow that differs quantitatively in character in each part of the brain substance. The results explain the "mosaic" character of damage to the brain substance in acute experimental arterial hypertension and the local nature of the neurological symptoms in patients with hypertensive crises.

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