EFFECT OF SHORT-TERM CEREBRAL ISCHEMIA ON THE MESENTERIC MICROCIRCULATION IN RATS

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The effect of cerebral ischemia produced by compression of both common carotid arteries on the mesenteric microcirculation was studied in experiments on rats. The extent and intensity of the microcirculatory disturbances were shown to depend on the duration of ischemia and of the postischemic period. The state of the systemic hemodynamics was compared with that of the mesenteric microcirculation. The possible mechanisms of the microcirculatory disturbances are discussed.

KEY WORDS: cerebral ischemia; microcirculation.

Cerebral ischemia is an extremely common condition in man, and in 50% of cases it is caused by a lesion of the main arteries to the head [3]. Clinical and experimental studies have shown that in this pathological form the blood supply to the myocardium may be insufficient [2] and the blood flow in the paretic and intact limbs may be reduced [1, 5]. It was decided to study the state of the microcirculation in organs remote from the brain during cerebral ischemia, for the transcapillary exchange which maintains local homeostasis takes place at the microcirculatory level. No data in the literature could be found on this problem.

The objects of this investigation were as follows: 1) to obtain experimental data on the state of the microcirculation in the mesentery during cerebral ischemia, and 2) to compare disturbances of the general hemodynamics and local disturbances of the microcirculation.

EXPERIMENTAL METHOD

Experiments were carried out on 40 male Wistar rats weighing 200-250 g. Cerebral ischemia was induced by compressing both common carotid arteries for 15, 30, and 60 min. This method, which considerably reduces the blood flow in regions of the brain supplied by the internal carotid artery, is the one usually adopted in rats [6-9]. After removal of the ligatures observations continued for 60 min. In control animals ligatures were applied to both common carotid arteries but were not tied. Pentobarbital anesthesia (5 mg/100 g body weight) was used in all the experiments and tracheostomy was performed. The systemic arterial pressure was determined electromanometrically after cannulation of the caudal artery and recorded on a San-ei polygraph. Biomicroscopy of the mesentery and parallel photographic recording were carried out on the MBI-15 microscope by the method generally adopted in the Laboratory of General Pathology and Experimental Therapy of the Institute.

EXPERIMENTAL RESULTS

Marginal stasis of the leukocytes (Fig. 1a) appeared 3 min after ligation of the common carotid arteries in venules 30-40 μ in diameter, and after 5 min the blood flow in venules with a diameter of 20 μ or more became granular in character. During this same period aggregates of erythrocytes appeared in the postcapillaries, and later (by the 7th-10th minutes) this contributed to the appearance of vessels filled with plasma only, so that discontinuity of the blood flow was observed in the capillaries and postcapillaries. At places in the vessels of the caliber mentioned above evidence of prestasis and stasis was observed. After

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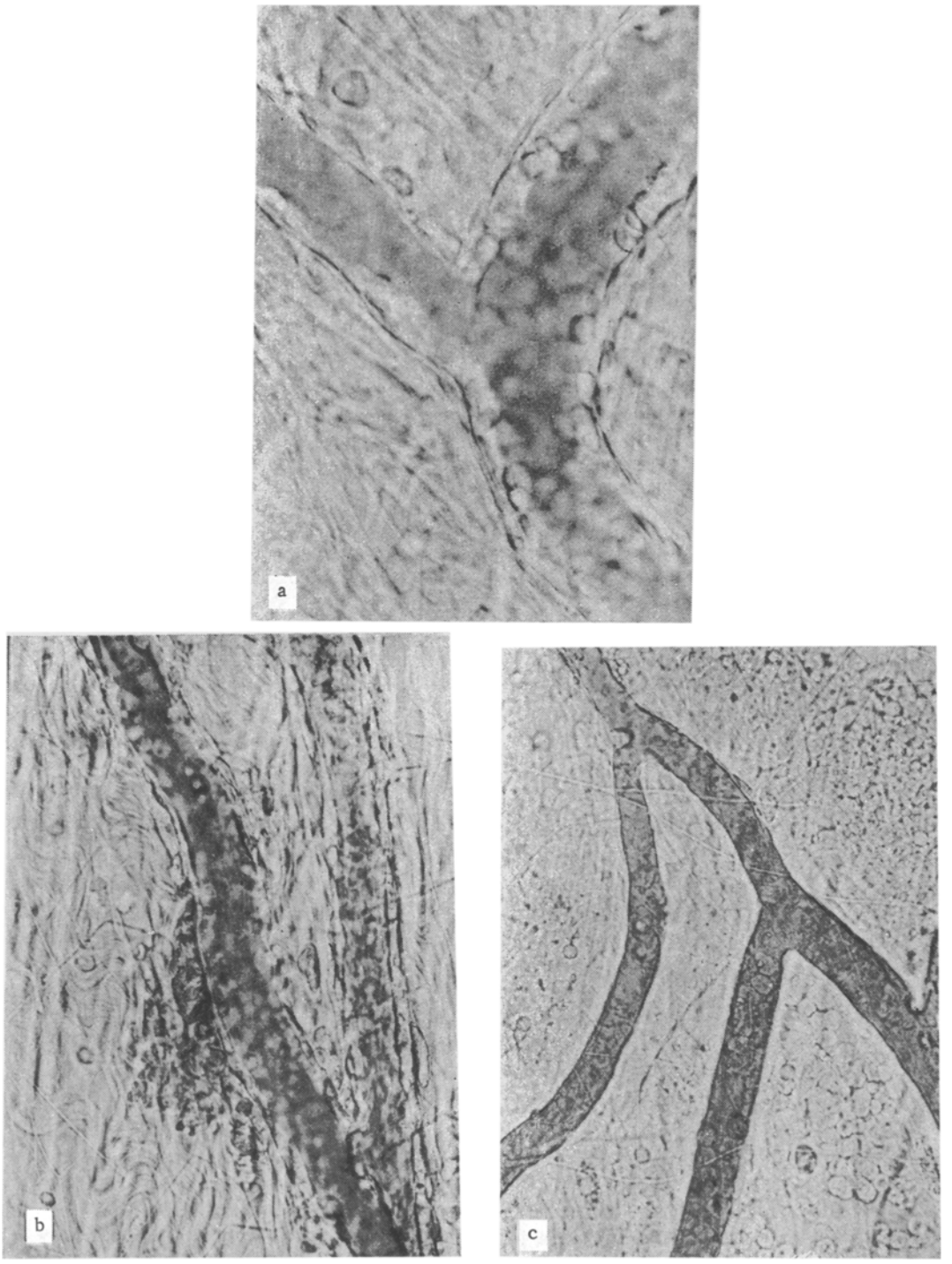

Fig. 1. State of the mesenteric microcirculation of rat during cerebral ischemia. a) Marginal stasis of leukocytes in venules of rat mesentery 3 min after ligation of both common carotid arteries (magnification 50×3.2); b) areas of extravesation around a mesenteric venule 15 min after ligation of both common carotid arteries (magnification 50×2.5); c) stasis in mesenteric microvessels of rat 60 min after ligation of both carotid arteries (magnification 50×2.5).

15 min of occlusion, extravasation of erthrocytes (Fig. 1b) began to appear around venules 20-30 μ in diameter, and after 20 min aggregation in the capillaries and postcapillaries increased. After longer periods of compression up to 60 min all the above-mentioned disturbances of the microcirculation were intensified and the signs of prestasis and stasis increased in severity (Fig. 1c).

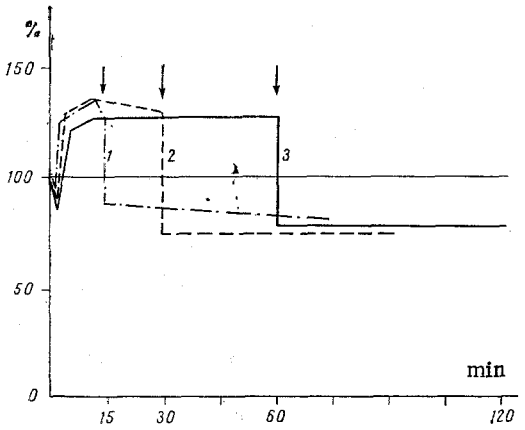

Fig. 2. Changes in systemic arterial pressure (BP) during ligation of common carotid arteries in rats. Abscissa, time (in min); ordinate, systemic BP (in %, original systemic BP taken as 100%). 1) Ligation of common carotid arteries for 15 min, 2) for 30 min, 3) for 60 min. Arrows indicate time of removal of ligatures.

Observations on the state of the mesenteric microcirculation after cerebral ischemia for 15 min showed that 5 min after removal of the ligatures from both common carotid arteries the biomicroscopic picture was the same as at the 15th minute of ligation, except that the number of postcapillaries and capillaries with stasis was increased. The formation of zones of extravasation around the postcapillaries was observed 15 min after the end of occlusion, and aggregation in capillaries, postcapillaries, and venules 20-30 μ in diameter was increased after 30-40 min. The state of the mesenteric microcirculation showed no significant change 60 min after removal of the ligatures.

The same disturbances of the microcirculation were observed in the mesentery 5, 15, 30, 40, 50, and 60 min after the end of occlusion of the carotid arteries in the experiments with cerebral ischemia for 30 min as in those with ischemia for 15 min at the same times, but extravasation from the postcapillaries was more severe, the areas of stasis were much more extensive, and stasis was observed also in the arterioles of the microcirculatory system.

Disturbances of the microcirculation at all stages of observation after the end of ligation of both carotid arteries for 60 min were even more severe than in the previous series of experiments. The blood flow after 60 min persisted only at the level of the larger arterioles and venules.

Analysis of changes in the diameter of the microvessels, based on the study of serial photographs, showed that ligation of the common carotid arteries causes statistically signifi-

TABLE 1. Constrictor Reaction of Arterioles in Rats After Ligation of Common Carotid Arteries

Duration of ligation, min	Diameter of arterioles, μ		
	10—15	15—25	25—30
Without ligation	12,8±0,23	18,0±0,3	27,3±0,5
½	12,2±0,15*	17,0±0,3*	25,1±0,41*
1	12,2±0,15*	17,2±0,25*	25,1±0,63*
3	12,8±0,45	18,0±0,33	28,2±0,37
15	13,8±0,45	18,1±0,33	27,8±0,39

*Difference from control group statistically significant, P<0.05.

cant constriction of the precapillaries, metarterioles, and arterioles 25-30 μ in diameter during the first 0.5-1 min (Table 1).

Measurement of the systemic arterial pressure during the experiments gave the following results (Fig. 2). During the first 0.5-1 min after ligation the systemic arterial pressure fell briefly in 77% of cases on average by 15-20% of its initial value. Later, starting from 1-3 min (in 80% of cases) or 5-7 min (in 20% of cases) after ligation, a hypertensive reaction developed, with a mean increase of 25-30% in BP. The duration of hypertension was: under 10 min in 7% of cases, under 15 min in 23%, under 30 min in 35%, and under 60 min in 35% of cases. Removal of the ligatures led to a decrease in systemic BP to 86% of its initial level after ischemia for 15 min and to 72% after ischemia for 30 and 60 min. The arterial pressure remained low throughout the remaining period of observation. At the end of the period of observation the mean systemic BP was: 78% of its initial level after cerebral ischemia for 15 min, 72% after ischemia for 30 min, and 74% after ischmia for 60 min.

The investigations thus showed that during cerebral ischemia substantial disturbances of the microcirculation in the mesentery were observed in the region supplied with blood by the internal carotid arteries and, in particular, after the end of ischemia. The severity of the microcirculatory disturbances depended on the duration of cerebral ischemia and on the length of the postischemic period. These changes could be due to several factors.

Comparison of the state of the systemic arterial pressure and the mesenteric microcirculation showed that the intensity and extent of the microcirculatory disturbances are influenced by the initial BP level, the duration of the hypertensive response (the longer the response, the smaller the disturbances), the degree of fall of BP in the postischemic period, and spasm of the mesenteric arterioles, due to the effect of baroreceptor stimulation, which may be a trigger factor for the development of the microcirculatory disorders. Similar responses of the arterioles in skeletal muscles, the intestine, and other organs in response to common carotid arterial occlusion have been demonstrated previously [4, 8].

It should be pointed out that simultaneous ligation of both common carotid arteries acted as a stressor for the animal and activated all the mechanisms of adaptation and injury, including those at the level of the microcirculatory system.

It can tentatively be suggested that, especially during long periods of cerebral ischemia, inorganic phosphate, lactic acid, incompletely oxidized metabolites, denatured proteins, and other substances, accumulating in the zone of ischemia and entering the blood stream, must also exert their action at the microcirculatory level in other organs.

LITERATURE CITED

1. G. S. Burd and M. Ya. Nekhlyudova, Zh. Nevropatol. Psikhiatr. im. S. S. Korsakova, No. 3, 425 (1971).
2. E. V. Shmidt, in: Vascular Diseases of the Nervous System [in Russian], Moscow (1975), pp. 348-355.
3. E. V. Shmidt, in: Vascular Diseases of the Nervous System [in Russian], Moscow (1975), pp. 358-435.
4. R. F. Bond and H. D. Green, Am. J. Physiol., 216, 393 (1969).
5. D. Bratko, Rev. Czech. Med., 20, 141 (1974).
6. J. Choki, T. Yamaguchi, Y. Takaya, et al., Stroke, 8, 376 (1977).
7. B. Eklöf and B. K. Siesjö, Acta Physiol. Scand., 86, 155 (1972).
8. B. Eklöf and B. K. Siesjö, Acta Physiol. Scand., 87, 69 (1973).
9. M. Fujishima, Y. Nakatomi, K. Tamaki, et al., J. Neurol. Sci., 33, 1 (1977).