EFFECT OF SEROTONIN ON VOLUME VELOCITY OF BLOOD AND pO_2 IN CERTAIN BRAIN REGIONS

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The effect of serotonin on the cerebral circulation has received inadequate study.

Whereas some workers [8-10] have described the vasoconstrictor effect of serotonin, others [11] in most cases observed dilatation of the blood vessels of the brain under the influence of this drug. Data relating to the effect of serotonin on the oxygen tension is the brain tissues are also contradictory [4, 5,7].

In the present investigation the effect of serotonin on the circulation and pO_2 in the brain tissues was studied by a combination of two methods: thermoelectric and polarographic.

EXPERIMENTAL METHOD

Experiments were carried out on 58 cats anesthetized with urethane (1 g/kg). The volume velocity of the blood flow was studied by a thermoelectric method [3] and pO_2 by a polarographic method [6].

Electrodes were introduced by means of a stereotaxic apparatus into the cortex of the occipital and parietal lobes, and also into the mesencephalic reticular formation in the region of the nucleus reticularis tegmentalis. Serotonin was injected intravenously, intramuscularly, and intraperitoneally in doses of between 50 and 10 mg/kg. The changes in the volume velocity of the blood flow and pO_2 were compared with changes in the systemic arterial pressure. The volume velocity of the blood flow and pO_2 were expressed percentages of their initial level.

EXPERIMENTAL RESULTS

Intravenous injection of serotonin in doses of 50 and 100 μg/kg always caused a decrease of the systemic arterial pressure, the volume velocity of the blood flow and pO_2 in the tissues of all regions of the brain studied (Fig. 1, a, b). The general arterial pressure was lowered by 40-80 %, and as a rule it was restored in the course of 8-20 min.

In the cortex of the occipital lobe the velocity of the blood flow was reduced by 70-90% under the influence of serotonin. The decrease continued for 9-11 min. In the parietal cortex the blood flow was reduced by 24-80%. This effect lasted 1-10 min. In the mesencephalic reticular formation the decrease in the volume velocity of the blood flow was less marked, but more prolonged than the changes in the blood flow in the cerebral cortex. The blood flow in the region of the nucleus reticularis tegmentalis was reduced by 18-50% and was restored after 7-20 min. In 4 of the 7 animals restoration of the blood flow did not take place during observations for 30 min. Sometimes after a decrease in the volume velocity of the blood flow caused by intravenous injection of serotonin, a phase of increased blood flow was observed. When the effect of serotonin on the circulation in the parietal cortex was studied, in 3 of 18 animals the preliminary fall in blood flow was followed by an increase in its value by 11-45%, lasting 2-18 min, and this increase in the cerebral blood flow took place against the background of continuing arterial hypotension. In two animals the blood flow was not restored to its original level, and in another two the restoration was incomplete.

After intravenous injection of serotonin, in all cases the value of pO_2 was reduced (Fig. 1, a, b). In the occipital cortex the value of pO_2 fell by 45-90%, returning to its initial level after 4-8 min. In the parietal cortex, pO_2 fell by 22-83% in the course of 1-8 min. In the mesencephalic reticular formation pO_2 fell by 30-40%. In two of five animals the initial level of pO_2 was not restored during observation for

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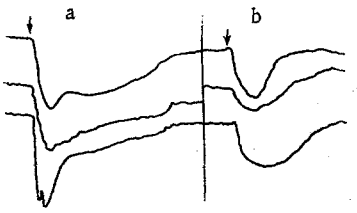

Fig. 1. Effect of intravenous injection of serotonin on velocity of blood flow and pO_2 in brain tissues. a) Occipital cortex; b) parietal cortex. Top curve – velocity of blood flow, middle – pO_2, bottom – general arterial pressure.

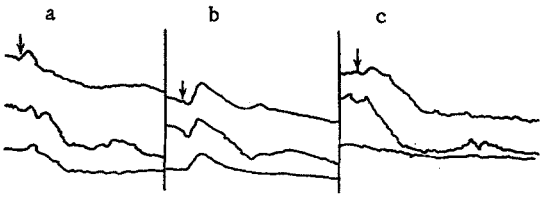

Fig. 2. Effect of intraperitoneal injection of serotonin on velocity of blood flow and pO_2 in tissues of the parietal lobe. Significance of curves as in Fig. 1.

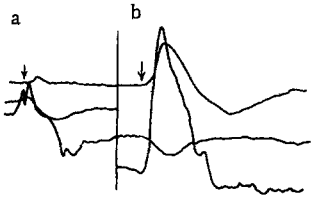

Fig. 3. Effect of intravenous injection of serotonin on velocity of blood flow and pO_2 in tissues of the parietal cortex of atropinized (a) and vagotomized (b) cats. Significance of curves as in Fig. 1.

30 min, and in three animals the decrease in pO_2 continued for 7-20 min. In some cases the decrease of pO_2 was followed by a phase of increase. Sometimes pO_2 was not restored for a long time; this was observed more commonly in the mesencephalic reticular formation. In the parietal cortex, in five of thirteen animals after the decrease of pO_2 it was increased by 20-60% for 4-7 min; the increase of pO_2 took place against the background of continuing arterial hypotension. In three of five animals pO_2 increased parallel to the increase in the blood flow. In two of thirteen animals the original level of pO_2 was not restored during observation for 30 min.

Intramuscular and intraperitoneal injection of serotonin in doses of 1.5 and 10 mg/kg caused a gradually increasing rise in the volume velocity of the blood flow and in pO_2 in the brain tissues, and a small decrease in the general arterial pressure (Fig. 2, a). In individual experiments after intraperitoneal injection of serotonin in a dose of 1 mg/kg a transient increase of arterial pressure (by 19%), of the volume velocity of the blood flow (by 15%), and of pO_2 (by 4%) was observed, followed by a decrease in the blood flow by 35% and in pO_2 by 12% (Fig. 2, b). The volume velocity of the blood flow and pO_2 fell against the background of recovery of the arterial pressure. In one experiment (cat No. 18), intraperitoneal injection of serotonin in a dose of 5 mg/kg caused practically no change of arterial pressure, whereas the volume of blood flow and pO_2 in the brain tissues fell by 56 and 62% respectively (Fig. 2c).

To study the role of the arterial hypotension arising under the influence of intravenous injection of serotonin in the reduction in the volume velocity of the blood flow and pO_2 in the brain tissues, experiments were carried out in which the vagus nerves were blocked by vagotomy or by intravenous injection of atropine in a dose of 2 mg/kg. Intravenous injection of serotonin in a dose of 50 μg/kg into atropinized animals caused dissimilar changes in arterial pressure, volume velocity of blood flow, and pO_2 in the tissues of the parietal cortex. In 4 of 6 animals the velocity of the blood flow was reduced by approximately the same degree as in unatropinized animals. In two cats an increase in the blood flow by 13 and 28%, lasting 1 and 3 min, was observed and was accompanied by a parallel, transient increase of arterial pressure by 18 and 20%. However, the level of pO_2 in these animals, after a transient increase by 5 and 20%, fell considerably (by 23 and 83%) (Fig. 3, a).

Intravenous injection of serotonin in a dose of 50 μg/kg into animals with divided vagus nerves also caused dissimilar changes. In six of thirteen animals the volume velocity of blood flow and the level of pO_2 fell. The arterial pressure was lowered in four of six cases, while in two cases it showed biphasic changes. In three of thirteen vagotomized animals serotonin caused an increase in the volume velocity of the blood flow by 33-66%, lasting 2-4 min (Fig. 3, b). The arterial pressure of these animals rose in one case, and showed biphasic changes in two. In four vagotomized animals, biphasic changes in the cerebral blood flow were observed, generally speaking, corresponding to the change in arterial pressure.

Under the influence of intravenous injection of serotonin into vagotomized animals, the pO_2 level in the brain tissues fell in all cases by 10-80%, and a fall in this index was observed even when the blood flow in the cortex was increased (Fig. 3, b). In other words, in atropinized and vagotomized animals the increase in volume velocity of blood flow under the influence of serotonin took place only when the arterial pressure was increased or when the phase of increased pressure was predominant. In no case was an increase in blood flow observed when the arterial pressure was lowered. Conversely, in some experiments (cat no. 28) biphasic changes in the blood flow took place under the influence of serotonin, with marked predominance of the phase of decrease, whereas the arterial pressure rose. The value of pO_2 fell in all cases, even when the cerebral blood flow was increased.

Hence, in experiments on cats, serotonin caused a decrease in the volume velocity of the blood flow and pO_2 in the brain tissues. Evidently the mechanism of these changes is highly complex. They may be considered as being associated with the Bezold-Jarisch reflex evoked by intravenous injection of serotonin. In these conditions the pressure at which blood is pumped into the brain vessels is reduced, and the oxygenation of the blood may also be reduced.

However, it is incorrect to attribute the decrease in volume velocity of the blood flow and in pO_2 entirely to the Bezold-Jarisch reflex. Experiments with intraperitoneal and intramuscular injection of serotonin, when in some cases the blood flow and pO_2 level fell independently of changes in the arterial pressure (Fig. 2, c), suggest that serotonin may also act directly on the brain vessels, reducing the volume velocity of the blood flow in them and, consequently, lowering pO_2 in the brain tissues. Experiments on atropinized and vagotomized cats, in which a decrease of pO_2 was observed in the conditions of an increased blood flow (Fig. 3), suggest that serotonin acts directly on the brain tissues, lowering the oxygen concentration in them.

It is difficult to explain the origin of the second wave of increase in the volume velocity of the blood flow and pO_2 which sometimes was observed after the phase of decrease. The wave of increase of blood flow and pO_2 possibly depends on dilatation of the brain vessels arising as a reaction to arterial hypotension. In the opinion of some investigators [1, 2], a decrease of arterial pressure, regardless of its cause, leads to dilatation of the brain vessels. A less probable suggestion is that the second wave of increase of the blood flow and pO_2 is a phase of direct action of serotonin on the cerebral circulation. The strongest evidence against this view is that the phase of increase of blood flow and pO_2 was not often observed, whereas the phase of decrease was observed in every case.

Hence, the decrease in volume velocity of the blood flow and in pO_2 in the brain tissues produced by serotonin is evidently associated with the influence of the drug on several links in the chain of regulation of the cerebral circulation, namely with a decrease in the blood flow to the brain associated with a decrease of arterial pressure, and with the direct effect of serotonin on the brain vessels and a decrease in the volume velocity of the blood flow in them. In addition, serotonin may possibly have a direct influence on brain tissues, lowering the oxygen concentration in them.

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