EFFECT OF SEROTONIN ON CUTANEOUS VASCULAR RESISTANCE IN GUINEA PIGS AT THE HEIGHT OF ACUTE RADIATION SICKNESS

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On the 7th day after irradiation with Co^{60} γ rays in a dose of 600 R (46 R/sec) 119 guinea pigs of both sexes weighing 230-350 g received an injection of serotonin creatine-sulfate (10 mg/kg) or 5-hydroxytryptophan (50 mg/kg). Injection of serotonin and 5-hydroxytryptophan into the irradiated animals led to an increase in their vascular resistance if hyperserotoninemia was observed. Serotonin can be assumed to have a role in the maintenance of vascular resistance, which it exerts through the platelets. Evidence of this was given by experiments in which the irradiated animals were treated with serotonin-enriched platelets.

Administration of serotonin, 5-hydroxytryptophan, and serotonin-enriched platelets to irradiated animals has been shown to increase the vascular resistance if hyperserotoninemia is observed. One possibility is that serotonin present in the platelets has a role in the mechanism maintaining vascular resistance.

In acute radiation sickness the vascular resistance to mechanical factors is considerably reduced. However, the pathogenesis of this disturbance of vascular resistance in radiation sickness has not been fully explained.

According to reports in the literature serotonin is concerned in the mechanism of maintenance of vascular resistance. At the height of acute radiation sickness, when the blood serotonin level is considerably reduced, so also is vascular resistance [1, 2]. Again, if irradiated animals are treated with serotonin, their vascular resistance is increased [4]. However, the mechanism of this effect of serotonin in maintaining vascular resistance and in determining its duration are not yet clear.

This paper describes the results of a study of the effect of serotonin on vascular resistance, depending on the time and method of its administration.

EXPERIMENTAL METHOD

In experiments on 119 guinea pigs of both sexes weighing 230-350 g the animals were irradiated with Co^{60} γ-rays in a dose of 600 R (46 R/sec). In series I the guinea pigs (52) were given an intraperitoneal injection of serotonin creatine-sulfate (Lawson, England; 10 mg/kg) or 5-hydroxytryptophan (50 mg/kg) on the 7th day after irradiation. In series II the guinea pigs (67) received an intravenous injection of 1 ml of a suspension of platelets from healthy animals in citrated plasma ($1.42 \cdot 10^9$ platelets/ml). In order to obtain serotonin-enriched platelets, some healthy animals received 5-hydroxytryptophan (50 mg/kg) 1 h before the blood was taken.

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TABLE 1. Effect of Serotonin on Platelet Count, Blood Serotonin Level, and Vascular Resistance of Irradiated Guinea Pigs

Indices studied	Control	1 h after injection of		2 h after injection of		4 h after injection of	
		serotonin	5-hydroxytryptophan	serotonin	5-hydroxytryptophan	serotonin	5-hydroxytryptophan
Platelet count (in %)	100	-	124	95	-	100	60*
Serotonin concentration (in %)	100	1057*	1085*	214	-	71	171
Cutaneous vascular resistance (in %)	100	200*	250*	117	-	121	155*

*$P < 0.05$ compared with control.

At intervals of 1, 2, and 4 h after injection of these substances the serotonin concentration was investigated by a spectrofluorometric method [6], the platelets were counted [3] with the aid of Fischer-Germer [5] diluting fluid, and the resistance of the cutaneous vessels of the abdominal wall to negative pressure (450 mm Hg, 2 min) was measured. The severity of the hemorrhages was assessed on a 5-point scale (0, 1, 2, 3, 4) and expressed as a percentage of the control. During the experiment the animals were anesthetized with Nembutal (30 mg/kg).

EXPERIMENTAL RESULTS

All the irradiated animals developed acute radiation sickness of medium severity ($LD_{90/30}$, thrombocytopenia, lowered vascular resistance, hyposerotoninemia).

It will be clear from Table 1 that 1 h after injection of serotonin into the irradiated animals the blood serotonin concentration and the vascular resistance both increased (by ten and two times respectively); meanwhile, 2 and 4 h after injection of serotonin these indices were the same as in the control.

An increase in the serotonin concentration (by seven times) and an increase in vascular resistance (by 60%) were observed 1 h after injection of 5-hydroxytryptophan into the irradiated animals. The effect of an increase in vascular resistance was also observed 4 h after injection of 5-hydroxytryptophan. At this time there was a further decrease in the platelet count and a tendency for the blood serotonin concentration to rise was observed under the influence of 5-hydroxytryptophan.

Injection of serotonin into the irradiated animals thus led to an increase in vascular resistance provided that hyposerotoninemia was observed (1 h after injection of serotonin), but when the serotonin level fell to its initial values, the vascular resistance was reduced.

Injection of 5-hydroxytryptophan led to an increase in vascular resistance which continued for 4 h. This phenomenon can be attributed to the prolonged elevation of the serotonin level in the platelets after administration of 5-hydroxytryptophan. It can be postulated that serotonin present in the platelets participates in the mechanism maintaining vascular resistance. This hypothesis was confirmed by the experiments of series II. Injection of platelets of healthy animals, not enriched with serotonin, caused no increase in vascular resistance in the course of 1 h, whereas injection of the same number of platelets, but with an increased serotonin content (see the section "Experimental Method"), was followed by an increase in the vascular resistance.

The experiments thus showed that serotonin plays a role in the maintenance of vascular resistance. In the writers' opinion, serotonin can act in this way through the platelets at the time of their adhesion and aggregation on the injured vessel wall. As a result, a high concentration of free serotonin is formed at the sight of injury, where it causes spasm followed by constriction of the injured vessel or a change in the microcirculation.

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