FUNCTIONAL STATE OF THE HEMOSTASIS SYSTEM DURING THE DEVELOPMENT OF EXPERIMENTAL SEROTONINOPENIA

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Endogenous serotonin participates in the arrest of bleeding from an injured vessel by constricting the lumen of the vessel and also by increasing aggregation of the platelets.

On the question of the possible role of serotonin in the mechanism of arrest of bleeding from a damaged blood vessel some investigators consider that serotonin acts as a vasoconstrictor [1, 5, 12], while others [6, 13, 14] consider that it affects the functional state of the clotting system of the blood. Some workers [17, 18], who completely reject any role of serotonin in hemostasis, justify their view by the fact that injection of reserpine, as a liberator of endogenous serotonin, into animals reduces the serotonin content in the blood and tissues, but at the same time it has no significant effect on the functional state of the blood clotting system [4].

For the foregoing reasons it was decided to study the functional state of the hemostasis system during the development of experimental serotoninopenia.

EXPERIMENTAL METHOD

Experiments were carried out on 95 Wistar rats of both sexes weighing 200-400 g. Serotoninopenia was produced by injecting reserpine (2 mg/kg) subcutaneously. From 18 to 20 h after injection of reserpine into the rats, investigations were made of the blood serotonin concentration, by a spectrofluorometric method [19], the number of platelets [11] and their aggregating properties [10], activity of factor XIII [2], tolerance of the fibrin clot to plasmin [3], the free heparin [8], the thrombin time [16], the plasma recalcification time [9], the resistance of the blood vessels in the skin of the abdominal wall, the bleeding time, and the volume of blood lost from the capillaries of the skin of the ear and caudal vein [7]. Blood was taken from the jugular vein into silicone-treated syringes, and mixed either with 3.1% sodium citrate solution or with 1.34% sodium oxalate solution in the ratio of 9:1. The animals were anesthetized with nembutal (30 mg/kg). Statistical analysis of the results was carried out with the aid of Student's t criterion.

EXPERIMENTAL RESULTS

As Table 1 shows, 18-20 h after injection of reserpine the blood serotonin concentration had fallen by 43%, the platelet count had risen by 16%, and platelet aggregation had increased by 63%. Meanwhile, in the animals of the experimental group, an increase of 42% in factor XIII activity, in the heparin concentration by 2.6 times, and in the tolerance of the fibrin clot to plasmin by 15% was observed. During the development of serotoninopenia in the rats, the resistance of the skin capillaries increased, and the volume of blood lost from the skin capillaries fell considerably (by 57%). However, the blood loss from the caudal vein of the experimental rats was 10 times higher than in the control. Other indices of the hemostasis system showed no significant changes.

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TABLE 1. Changes in Indices of Hemostasis in Rats during Development of Experimental Serotoninopenia

Index	Control	Expt.
Blood serotonin concentration (in μg/ml)	0.28	0.16*
Platelet count (in thousands/mm^3)	704	820*
Aggregation of platelets (in mV)	0.76	1.24*
Activity of factor XIII (in %)	100	142*
Tolerance of fibrin clot to plasmin (in min)	125	144*
Blood heparin concentration (in %)	100	260*
Thrombin time (in sec)	29	33
Plasma recalcification time (in sec)	118	109
Resistance of skin capillaries (degrees)	II	I*
Bleeding time (in sec):		
from capillaries	166	161
from vein	157	175
Volume of blood lost (in ml):		
from capillaries	0.014	0.006*
from vein	0.18	1.96*

*Significance of differences $P \leq 0.05$.

During prolonged liberation of serotonin from the tissues and platelets by the action of reserpine, conditions are created for the action of the free form of serotonin, which stimulates aggregation of the platelets, increases their number, and also apparently increases activity of factor XIII. However, the free serotonin is in the plasma only for a very short time, for it is accessible to the action of monoamine oxidase, which gradually reduces the serotonin concentration. With a decrease in the blood serotonin concentration, the free heparin concentration rises. The increase in resistance of the skin vessels and the decrease in volume of blood lost from the capillaries in the present experiments can be attributed to an increase in the number of platelets and, in particular, to an increase in their aggregating power and the activity of factor XIII, by virtue of which a lasting primary platelet thrombus is formed at the site of injury of the small blood vessel. After injury to larger vessels, the formation of platelet thrombi is insufficient to prevent bleeding. Arrest of bleeding from large vessels takes place through the formation of a coagulation thrombus. Investigations have shown that after injection of reserpine, producing serotoninopenia, the heparin concentration rises, but this cannot influence the formation of the coagulation thrombus. In addition, participation of serotonin as a vasoconstrictor and antiheparin agent [15] is another likely additional mechanism leading to arrest of bleeding from an injured large blood vessel.

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