PROPHYLAXIS OF EXPERIMENTAL THROMBOSIS IN SPLENECTOMIZED ANIMALS BY INTRAVENOUS INJECTION OF FIBRINOLYSIN AND HEPARIN

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It was shown in a previous work [1] that complete splenectomy causes a prethrombotic condition characterized by an increase in fibrinogen concentration and a decrease in fibrinolytic activity in rats. Without exception, injecting such animals intravenously with moderate doses of thrombin caused death from thrombosis, in contrast to control animals, which survived under these conditions.

The present work was a study of the possibility of preventing thrombosis in splenectomized rats by intravenous infusion of fibrinolysin and a combination of fibrinolysin and heparin.

EXPERIMENTAL METHOD

In this work we used a fibrinolysin preparation developed for clinical administration and so recommended by the laboratory. The preparation was dissolved in physiological NaCl, 150 units per ml. The fibrinolysin solution was injected into the jugular vein in a dose of 1 ml per 100 g of body weight. The fibrinogen concentration in the blood and the plasma fibrinolytic activity were determined by Bidwell's method [4].

We used 195 white rats weighing from 160 to 170 g in the experiment. The spleen was removed under aseptic and ether anesthesia. The control was animals subjected to laparotomy without removal of the spleen.

EXPERIMENTAL RESULTS

As may be seen from Table 1, 7 days after removal of the spleen the fibrinogen concentration in the experimental animals was elevated in comparison with the control, while plasma fibrinolytic activity was depressed.

TABLE 1. Fibrinogen Concentration and Fibrinolytic Activity of The Blood in Splenectomized Rats after Injection of Fibrinolysin

Nature of expt.	No. of animals	Fibrinogen concentration on 7th day of expt. (mg-%)	Fibrinolytic activity on 7th day of expt. (%)	Fibrinogen concentration (mg-%) after inj. of fibrinolysin			Fibrinolytic activity (%) after injection of fibrinolysin		
				After 5 min*	After 30 min	After 90 min	After 5 min	After 30 min	After 90 min
Splenectomy	37	600	7	390	337	268	25	16	1.5
Laparotomy (control)	20	485	24	380	427	470	0	2	8

*Biometric processing of the data on fibrinogen concentration on the 7th day of the experiment and 5 min after injection of fibrinolysin: $P < 0.001$ for splenectomy and $P < 0.01$ for laparotomy.

TABLE 2. Survival Rate Among Splenectomized Rats after Injection of Thrombin and Subsequent Administration of Fibrinolysin and Fibrinolysin and Heparin

Preparations administered	Nature of experiment	Thrombin dose (ml)	Heparin dose (units/100 g)	Fibrinolysin dose (units/100 g)	Number of animals	
					Total	Died
Fibrinolysin	Splenectomy	1.2-1.6	–	150	20	20
Heparin and fibrinolysin (jointly)	"	1.2-1.6	4.5-8.5	150	26	0
Heparin and fibrinolysin (successively)	"	1.2-1.6	17	150	10	4
Heparin	"	1.2-1.6	6.25-8.5	–	14	9
"	"	1.2-1.6	17	–	10	3
Physiological solution	"	1.2-1.6	–	–	11	11
The same	Control	1.2-1.6	–	–	10	0

TABLE 3. Fibrinogen Concentration and Fibrinolytic Activity of the Blood in Splenectomized Rats after Administration of Heparin and Heparin and Fibrinolysin

Preparations administered	No. of animals	Fibrinogen concentration on 10th-14th day of experiment (mg-%)	Fibrinolytic activity on 10th-14th day of experiment (%)	Fibrinogen concentration (mg-%) after injection of drugs			Fibrinolytic activity after injection of drugs (%)		
				After 5 min*	After 30 min	After 90 min	After 5 min	After 30 min	After 90 min
Heparin	10	486	5	392	382	409	4.7	3.8	3.1
Heparin and fibrinolysin	16	488	4.5	266	226	232	43	19	28
Fibrinolysin	11	585	4	393	319	–	26	18	2

*Biometric processing of the data on fibrinogen concentration: $P \leq 0.05$ on injection of heparin, $P < 0.05$ on administration of heparin and fibrinolysin, and $P < 0.01$ on administration of fibrinolysin.

Intravenous injection of these animals with fibrinolysin led to a decrease in fibrinogen concentration and a brief 15-20) minsharp rise in plasma fibrinolytic activity. In the control animals injection of the same dose of the drug produced a relatively smaller and briefer (5 min) change in fibrinogen concentration; in contrast to the splenectomized animals, the control animals exhibited a sharp drop in or complete disappearance of plasma fibrinolytic activity.

On the basis of previously published data [2], the results obtained enable us to assume that as a result of splenectomy the experimental animals lost their antifibrinolysin protective reaction, which appeared to its full extent in the control rats. In this connection it might be expected that intravenous administration of fibrinolysin to splenectomized animals would have a prophylactic effect against thrombosis provoked by subsequent intravenous injection of thrombin.

As may be seen from the data presented in Table 2, this hypothesis was not confirmed. Injection of fibrinolysin alone did not protect animals in this type of prethrombotic condition from thrombosis. The most marked prophylactic effect was obtained from a combination of fibrinolysin with small doses of heparin (administered simultaneously). Successive administration of these two drugs (the fibrinolysin 5 min after the heparin) was less effective (Table 2).

The maximal prophylactic effect of joint administration of fibrinolysin and heparin is shown by the data cited in Table 3. The heparin dose was 17 units/100 g and the fibrinolysin dose 150 units/100 g.

As may be seen from the data presented, in the prethrombotic condition caused by complete splenectomy combined intravenous injection of fibrinolysin and heparin produces a decrease in fibrinogen concentration and sharply increases the fibrinolytic activity of the blood. The effect of administration of fibrinolysin alone is not as marked; this is true to an even greater extent of heparin. The phenomenon in question apparently results from the fact that heparin introduced in vivo in appropriate doses eliminates the activity of the antifibrinolysin present in the blood, which prevents fibrinolysis when fibrinolysin appears in the blood stream [3].

LITERATURE CITED

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
