Thus retention of Na^+ and acceleration of re-entry of K^+ are observed in erythrocytes, preloaded with Na^+ and deprived of K^+, in borderline and essential hypertension, so that the membrane defect can be regarded as a characteristic manifestation of primary hypertension [1, 2, 9]. Consequently, the method suggested by Garay and Meyer [7] can be used as a differential diagnostic test for the study of hypertension and for the institution of preventive measures.

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EFFECT OF HEPARIN ON THE BLOOD VESSEL–PLATELET STAGE OF THE HEMOSTASIS SYSTEM AND PATHOGENETIC CORRECTION OF RESULTING DISTURBANCES

I. K. Tlepshukov

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KEY WORDS: heparin; blood vessel–platelet stage of the hemostasis system; correction; deaggregating agent.

Heparin is one of the anticoagulants most frequently used in clinical practice, and its effectiveness is determined by its antithrombin and antithromboplastin actions, and inhibition of the conversion of fibrinogen into fibrin. However, by preventing blood clotting, heparin induces intravascular aggregation of platelets [4] and depresses the antiaggregating activity of the vessel wall [1], and this is an adverse side effect. Functional injuries to the vessel wall due to depression of its antiaggregating activity in such cases may be a component in the pathogenesis of the ricochet thromboses that arise when heparin is discontinued.

The aim of this investigation was to study the effect of intravenous injection of heparin on the blood vessel–platelet stage of the hemostasis system and to seek ways of pharmacologic correction of the resulting disturbances.

EXPERIMENTAL METHOD

Experiments were carried out on 36 male Wistar rats weighing 180-220 g. Heparin solution (from Gedeon Richter, Hungary) was injected into the femoral vein of the anesthetized animals (40 mg/kg pentabarbital sodium, intraperitoneally) in a dose of 750 U/kg body weight. Intravascular platelet aggregation was determined 10 min after injection of heparin by the method in [6], the antiaggregating activity of the vessel wall was investigated by the method in [5], and the number of platelets in the peripheral blood was counted on an AI-131 cell counter (Analysis Instruments, Sweden). The antiaggregating activity of the vessel wall was judged from the degree of inhibition of platelet aggregation induced by platelet-enriched plasma, obtained from the blood of donor rats, taken from the abdominal aorta and stabilized with 3.14% sodium citrate solution in the ratio of 9:1. The disodium salt of ADP (from Reanal, Hungary), in a final concentration of 10^{-5} M was used as aggregation inducer. The

Department of Radiation Pathophysiology, Scientific-Research Institute of Medical Radiology, Academy of Medical Sciences of the USSR, Obninsk.

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TABLE 1. Effect of Heparin on Blood Vessel-Platelet Stage of Hemostasis System

Experimental conditions	Index of intravascular platelet aggregation	Antiaggregating activity of vessel wall, %	Platelet count, 10^9/liter
Control	1,1±0,1	30±4,5	769±37,6
Heparin	2,9±0,3**	6±3,3**	203±23,4**
Heparin + complex	1,5±0,1*	44±3,9	456±118,2

Note. *P < 0.05, **P < 0.01.

aggregating activity of the vessel wall was expressed as a percentage of inhibition of ADP-induced platelet aggregation. The results were subjected to statistical analysis and the significance of differences was estimated by Student's t test.

EXPERIMENTAL RESULTS

Intravascular platelet aggregation appeared 10 min after injection of heparin into the animals: The index of intravascular platelet aggregation was almost trebled compared with the initial value, the antiaggregating activity of the vessel wall was reduced fivefold, and the blood platelet count was reduced more than threefold (Table 1).

To correct the disturbances of function of the blood vessel–platelet stage of the hemostasis system induced by heparin, we used a combination of drugs which, on theoretical grounds and on the basis of previous investigations aimed at restoring antiaggregating activity of the vessel wall when depressed by the use of other agents, can abolish the unfavorable side effects of heparin [3]. For this purpose heparin was injected simultaneously with deaggregating agents: dipyridamole, which can restore the antiaggregating activity of the vessel wall, and nicotonic acid, which can prevent depression of the antiaggregating activity of the vessel wall, as has been demonstrated on models with hyperadrenalinemia [2, 3].

Intravascular platelet aggregation 10 min after injection of a combination of drugs, consisting of 750 U heparin, 2.5 mg dipyridamole, and 1.5 mg nicotinic acid per kilogram body weight, into the animals was reduced by 50% compared with that observed after injection of heparin alone. The antiaggregating activity of the vessel wall was not reduced under these circumstances, and the platelet count was more than twice that observed after injection of heparin.

Consequently, heparin gives rise to adverse side effects on function of the blood vessel–platelet stage of the hemostasis system, blocking the clotting system of the blood, on the one hand, and increasing the risk of formation of a platelet thrombus as a result of depression of the antiaggregating activity of the vessel wall and induction of intravascular platelet aggregation, on the other hand. Deaggregating agents, preventing functional disturbances of the blood vessel–platelet stage of the hemostasis system during hyperadrenalinemia have the same action aso after injection of heparin. During heparin therapy, in order to prevent its adverse side effects, a combination of drugs consisting of the deaggregating agents dipyridamole and nicotinic acid, which can prevent the onset of functional disturbances affecting the blood vessel–platelet stage of the hemostatis system and can reduce the risk of development of thromboembolic complications, must be included in the treatment schedule.

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EFFECT OF FERRIC CHLORIDE ON DENERVATED SKELETAL MUSCLES

N. P. Rezvyakov, R. R. Islamov,
A. A. Salakhov, and É. G. Ulumbekov

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The transferrin-like glycoprotein sciatin [6, 8], the iron-transporting protein transferrin [6, 7, 10], and even trivalent ferric ions [5, 9] have a differentiating effect on myogenic skeletal muscle cells developing *in vitro*. In particular, 10-100 μM of Fe^{+++} increases the number of clustered acetylcholine receptors on the surface of muscle tubes [5]. Injection of transferrin bound with Fe^{+++} into a denervated skeletal muscle *in situ* also changes the expression of acetylcholine receptors [11], thereby partially preventing the development of a denervation syndrome with respect to this feature. These facts suggested that the factor responsible for neurotrophic control of skeletal muscle is transferrin. To determine the mechanism of the effect of transferrin and also of Fe^{+++} on muscle, it was decided to study the action of these factors on skeletal muscles.

This paper givea the results of a study of the effect of inorganic iron on some histochemical and morphometric characteristics of denervated skeletal muscles.

EXPERIMENTAL METHOD

Experiments were carried out on 20 non-inbred male albino rats in which the sciatic nerve was divided unilaterally under ether anesthesia under sterile conditions, and on 10 rats which, after division of the nerve, received an intraperitoneal injection of 10^{-6} M $FeCl_3$ (1 ml/100 g body weight) daily for 3 days. The animals were weighed at the beginning and end of the experiments. The rats were decapitated under deep ether enesthesia. The soleus and plantaris muscles were isolated and weighed, and myosin ATPase activity [4] and succinate dehydrogenase (SDH) activity, with the aid of nitro-BT [2], were determined in frozen sections 10 μ thick. The relative number of muscle fibers of different types was counted and the area of their cross section measured in histological sections. Muscle homogenates with equal protein content were subjected to polyacrylamide gel disc electrophoresis [1]. Lactate dehydrogenase (LDH) activity was determined and the gels were photographed. Densitometry of the negatives was done on an IFO-451 dual-beam recording microphotometer. The results were subjected to statistical analysis by the t test [3]. A 0.05 level of significance was adopted.

TABLE 1. Relative Number (in %) and Area of Cross Section (in μ^2) of Muscle Fibers in Control and Experimental Animals ($X \pm S_X$)

	Soleus muscle		Plantaris muscle	
	I	II	I	II
Control	78,2±2,6 2400±112,8	21,8±2,6 2960±75,3	16,8±1,7 2722,6±92,9	83,2±1,7 3162,4±89,5
Experimental	80,6±3,1 2594,4±102,6	19,8±3,2 3562,8±86,2*	27,6±3,2* 2612,6±78,4	72,3±3,2 3224,1±149,5

I) Type I of muscle fibers, II) type II.
Note. Asterisk indicates significant differences compared with control.

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