served rarely, and only in undeveloped vascular networks. In most vascular networks there is a gradual disturbance of the blood flow, depending on the duration of reperfusion.

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Na^+-K^+ COTRANSPORT IN THE ERYTHROCYTE MEMBRANE IN PATIENTS WITH ESSENTIAL AND SYMPTOMATIC (RENAL) HYPERTENSION

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Changes in permeability of erythrocyte membranes for Na^+ and K^+ ions have been observed in patients with essential hypertension and in its experimental model, namely, spontaneous hypertension in rats. Changes in permeability of erythrocyte membranes also have been discovered in persons with normal blood pressure but whose parents are hypertensive [2, 7]. Changes in this kind are not found in symptomatic arterial hypertension, whether experimentally or clinically [8, 9].

The aim of this investigation was to study changes in permeability of erythrocyte membranes for Na^+ and K^+, with particular reference to Na^+-K^+ cotransport in erythrocytes of patients with essential hypertension and with sympotomatic (renal) hypertension, taking hereditary factors into account.

EXPERIMENTAL METHOD

Erythrocyte permeability was studied in 38 patients with stage I and II of essential hypertension (WHO classification; 12 women and 26 men aged from 30 to 58 years), in 12 patients with symptomatic (renal) hypertension (seven women and five men aged from 40 to 59 years), in nine patients (two women and seven men aged from 26 to 54 years) in whom a raised blood pressure (BP) up to the higher limit of normal was observed episodically (borderline hypertension), and in 15 persons (three women and 12 men aged from 34 to 49 years)

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TABLE 1. Movement of Cations in Erythrocytes of Patients with Hypertension (M ± m)

Group of subjects	Initial concentration of cation, mmole/liter of erythrocytes		Concentration of cation after treatment with 0.1 mM PCMB, mmoles/liter of erythrocytes		Rate of outflow of Na^+ from erythrocytes, mmoles/liter of erythrocytes/h	Rate of inflow of K^+ into erythrocytes, mmoles/liter of erythrocytes/h	Ratio of between flow rates of Na^+ and K^+
	Na^+	K^+	Na^+	K^+			
group (n•23)	18,70±1,01	87,44±4,23	96,43±4,23	9,72±1,76	2,66±0,34	0,82±0,04	3,41±0,47
Normal subjects with family history (n = 15)	20,20±1,27	91,30±4,84	97,04±4,83	10,37±1,86	2,04±0,22	0,98±0,07	2,1±0,29*
Patients with borderline hypertension (n = 9)	16,88±0,97	93,24±5,26	98,24±5,36	12,94±2,09	1,90±0,07*	1,21±0,17*	1,86±0,42*
Essential hypertension (n = 38)	17,24±0,83	88,33±3,09	103,00±8,48	11,94±1,04	1,84±0,20*	1,16±0,16*	1,74±0,34**
Symptomatic (renal) hypertension (n = 12)	19,37±0,85	91,00±5,79	100,6±7,41	13,07±2,89	2,69±0,12	0,87±0,12	3,05±0,48

Note. *P < 0.05, **P < 0.01 compared with control.

with normal BP, whose parents (one or both), according to the medical history, had essential hypertension.

The control group consisted of 23 clinically healthy persons (8 women and 15 men aged from 31 to 51 years), with no family history of raised BP or death from hypertension. Patients with essential and renal hypertension received the usual hypotehsive therapy, but all medication was withheld on the 3 days before the investigation. Permeability of the erythrocyte membrane for Na^+ and K^+ was studied by the method in [8]. Na^+ and K^+ concentrations in the erythrocyte hemolysate were determined by flame photometry. Hemoglobin was determined spectroscopically at 540 nm as cyanohemoglobin in order to allow for the erythrocyte concentration in the samples tested. The rate of flow of Na^+ and K^+ was calculated by linear regression analysis [5].

EXPERIMENTAL RESULTS

The sodium salt of p-chloromercuribenzoic acid (PCMB) has two significant effects on the flow of monovalent cations in erythrocytes: It increases passive permeability and inhibits active transport [10], with the result that the Na^+ concentration in erythrocytes rises but the K^+ concentration falls. During incubation of these cells in Ringer's solution they reacquire the ability to restore the steady-state concentration of Na^+ and K^+. Reciprocal movement of the Na^+ and K^+ flows in erythrocytes (Na^+-K^+ cotransport) is a linear function of time and provides a measure of the erythrocyte membrane permeability [8].

The rate of outflow of Na^+ from erythrocytes loaded with Na^+ and deprived of K^+, in patients with essential hypertension and with borderline hypertension was reduced compared with the control. In patients with hypertension of renal origin the outflow of Na^+ from erythrocytes loaded with Na^+ and deprived of K^+ was the same as in the control. The rate of inflow of K^+ into erythrocytes loaded with Na^+ and deprived of K^+, on the other hand, was significantly higher in patients with essential and borderline hypertension than in control. No abnormalities were found in patients with renal hypertension (Table 1).

Assessment of permeability of the erythrocyte membranes in terms of Na^+-K^+ cotransport parameters revealed a distinct difference in the ratio of Na^+ and K^+ flow rates between patients with essential hypertension and persons in the control group ($P < 0.01$).

According to data in the literature [8], an inversely proportional relationship is observed between the ratio of the Na^+ and K^+ flow rates in the erythrocytes and BP in patients with essential hypertension. However, comparative analysis of the Na^+-K^+ cotransport system in the erythrocytes and blood pressure in patients with essential hypertension did not reveal any such relationship.

Comparison of the Na^+-K^+ contransport system in the erythrocytes of subjects with a family history of hypertension and in subjects of the control group revealed a difference in the ratio of Na^+ and K^+ flow rate: In subjects with a family history of hypertension this value was 2.10 ± 0.29, compared with 3.41 ± 0.47 in the control. Similar results were obtained by other workers also, studying permeability of erythrocyte membranes in healthy children whose parents had arterial hypertension [6, 7].

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

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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

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