NEW BIOMEDICAL TECHNOLOGIES

Role of Ionic Transport in Regulation of Hemoglobin Affinity for Oxygen in Diabetes Mellitus

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The rate of Na^+/H^+ exchange is increased by 24%, activities of Ca-dependent K^+ channels is increased by 13%, and activity of erythrocyte Ca^{2+}-ATPase decreased by 17% in patients with diabetes mellitus concomitant with essential hypertension in comparison with patients with essential hypertension without disorders of carbohydrate metabolism. Changes in activity of Na^+/H^+ exchange, Ca-dependent K^+ channels, and erythrocyte Ca^{2+}-ATPase and increased oxygen affinity of hemoglobin are due to increased glucose concentration in the plasma and are leveled by olifen.

Key Words: *diabetes mellitus; Na^+/H^+ exchange; Ca-dependent K^+ channels; erythrocyte Ca^{2+}-ATPase; olifen*

Common pathogenetic mechanisms of essential hypertension (EH) and diabetes mellitus (DM) are demonstrated in many studies. Inhibition of Ca^{2+}-ATPase and accumulation of intracellular Ca^{2+} were shown in patients with hyperglycemia [6]. Correction of blood glucose concentration with exogenous insulin restores Ca^{2+}-ATPase activity [7]. The increase in blood glucose concentration activates Na^+/H^+ exchange in lymphocytes and modulates blood pressure. EH is associated with changes in hemoporphyrin conformation determining increased oxygen affinity of hemoglobin; disorders in the regulation of intracellular pCa and erythrocyte pH were detected [1]. Changes in hemoporphyrin conformation in EH determine decreased Po_2 and increased Pco_2, which cause tissue hypoxia.

We investigated the mechanisms underlying regulation of intracellular pCa and erythrocyte pH and oxygen affinity of hemoglobin in DM concomitant with EH and during olifen treatment.

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MATERIALS AND METHODS

Venous blood was obtained from donors, patients with type II DM and EH, and patients with EH. Whole blood and erythrocytes were analyzed [4]. Changes in the hemoglobin iron atom affinity for oxygen were recorded by combined dispersion spectroscopy [1,2]. The rate of Na^+/H^+ exchange was evaluated by potentiometry [6], Ca^{2+}-ATPase activity in erythrocytes [4] and activity of Ca-dependent K^+ channels [5] were measured. Olifen (hypoxene), poly(-2,5-dihydrooxyphenilene)-thiosulfuric acid sodium salt was used.

RESULTS

In diabetics with EH the rate of Na^+/H^+ exchange and activity of Ca-dependent K^+ channels were higher and activity of Ca^{2+}-ATPase was lower than in EH patients without disorders in carbohydrate metabolism (Table 1).

Activity of Na^+/H^+ exchange and Ca-dependent K^+ channels increased and Ca^{2+}-ATPase activity decreased with increasing blood glucose content; the maximum shifts were observed at glucose concentra-

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TABLE 1. Ionic Homeostasis of Erythrocytes in EH Patients with and without Carbohydrate Metabolism Disorders (*M*±*m*)

Parameter	EH (*n*=20)	EH+DM (*n*=20)
Activity of Na^+/H^+ exchange, μmol Na^+/min	191.4±12.6	254.8±11.2*
Activity of Ca-dependent K^+ channels, μmol K^+/min	4.1±0.7	5.4±0.5
Activity of Ca^{2+}-ATPase, μmol Ca^{2+}/min	138.4±17.1	123.1±15.0

Note. *p<0.01 compared to EH group.

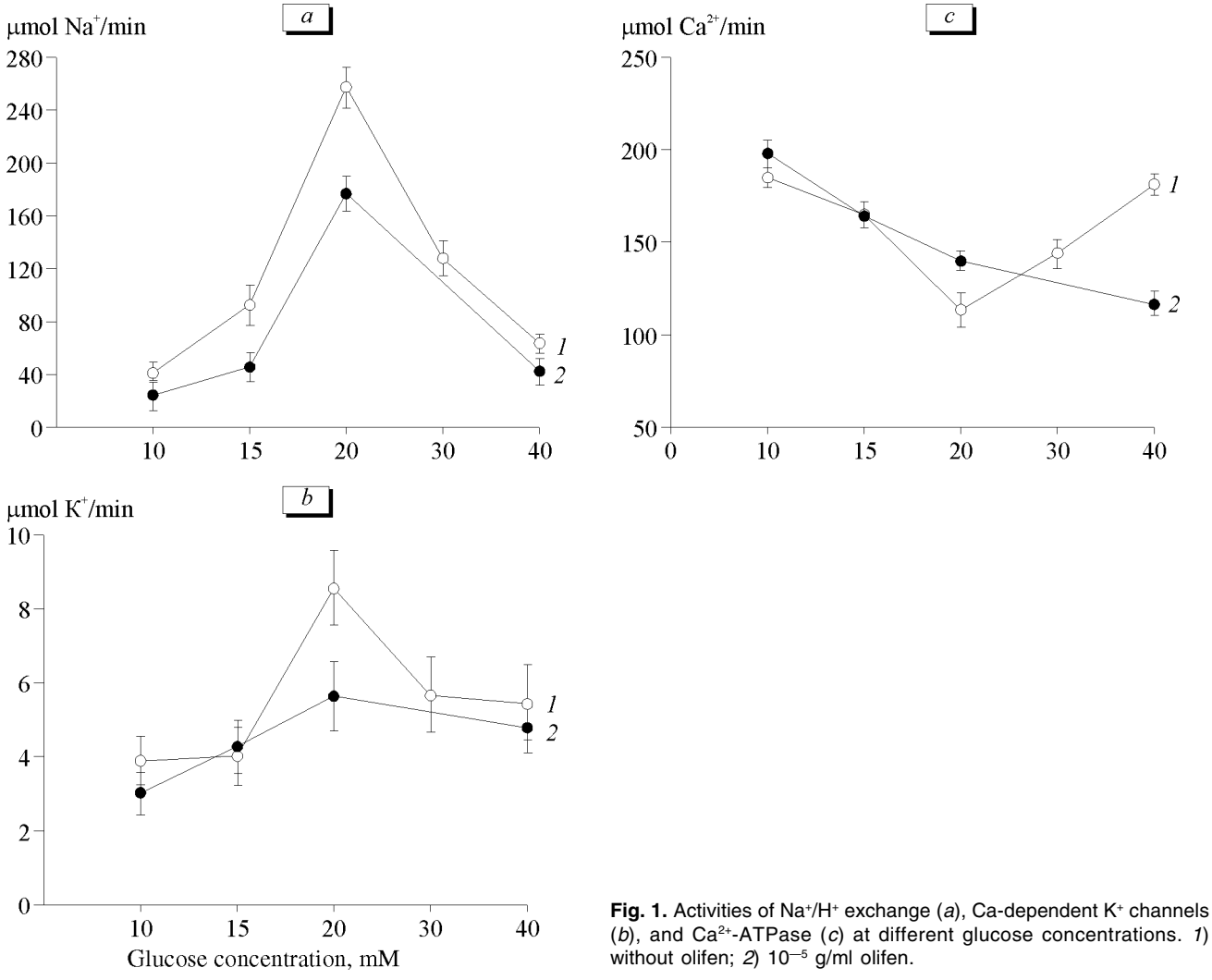

Fig. 1. Activities of Na^+/H^+ exchange (*a*), Ca-dependent K^+ channels (*b*), and Ca^{2+}-ATPase (*c*) at different glucose concentrations. *1*) without olifen; *2*) 10^{-5} g/ml olifen.

tion of 20 mM (Fig. 1). Olifen corrected changes in erythrocyte ionic homeostasis induced by high glucose concentrations (Fig. 1).

Our experiments showed that the increase in glucose concentration led to changes in oxygen affinity of hemoglobin. This parameter was 180±8% of the control level at glucose concentration of 20 mM. Olifen dose-dependently corrected these shifts: in the presence of 20 mM glucose, oxygen affinity of hemoglobin was 157±8, 121±8, and 100±8% of the control in the presence of olifen in concentrations 10^{-6}, 10^{-5}, and 10^{-4} g/ml, respectively.

Spectroscopy demonstrated higher intensity of combined dispersion peaks of hemoglobin porphyrin at glucose concentration of 20 mM in the presence of 10^{-4} g/ml olifen compared to that in the presence of glucose alone (Fig. 2).

Hence, the increase in plasma glucose concentration is paralleled by an increase in oxygen affinity of hemoglobin, which can modulate the content of O_2 and CO_2. Olifen not only reduced oxygen affinity of hemoglobin (which stimulates oxygen release into plasma and stimulates tissue respiration), but also restore activities of Na^+/H^+ exchange, Ca-dependent K^+

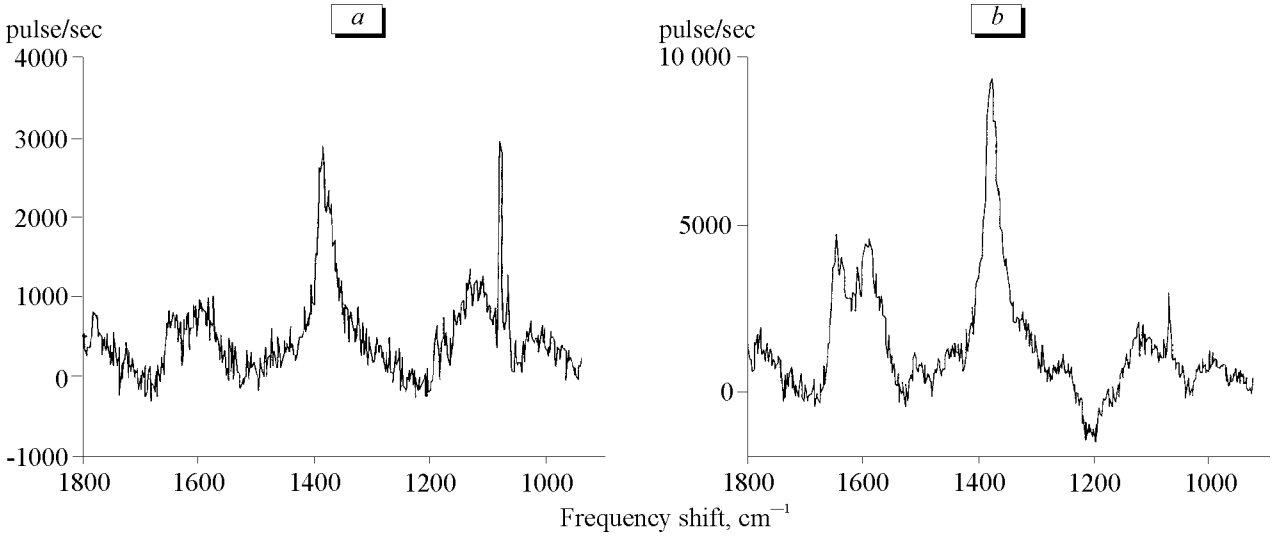

Fig. 2. Characteristic spectrum of erythrocyte hemoglobin porphyrin spectrum in the presence of 20 mM glucose and during combined treatment with glucose and olifen (10^{-4} g/ml, *b*). Combination diffusion spectroscopy.

channels, and Ca^{2+}-ATPase (erythrocyte ionic homeostasis), which is important in the therapy of DM.

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