EPITHEORESE KLINIKES FARMAKOLOGIAS
KAI FARMAKOKINETIKES, INTERNATIONAL
EDITION 16: 42 (2002)

Stimulation of the Na^+-H^+ Exchanger by Insulin anc Glucose in Human Monocytes

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AIM

Na^+-H^+ exchanger (NHE) is a basic regulator of intracellular pH (pHi).Under physiological conditions, the most important factor-regulator of the NHE is intracellular pH, whose decrease stimulates the NHE activity. This stimulation is a result of the intense dependence of pHi from the exchange rate and allows the exchanger to react even to small changes of pH. NHE activity is also regulated by various extracellular factors, including different growth factors, hormones and mechanical stimulation. Changes of intracellular pH are in accord with changes in intracellular paths of signal transmission which conduct to cell division or apoptosis. NHE function can be reversibly inhibited by amiloride analogs. Recently, such an analog (HOE642) has been tested clinically for the protection of myocardium during ischemic episodes. Besides, it has been reported that amiloride's analogues inhibit leukemic cell proliferation. Recently, our research team reported that insulin, adrenaline, leptin and increased glucose concentration stimulate NHE in human erythrocytes. These results show that NHE stimulation is possibly involved in diabetes vascular complications. Monocytes-macrophages play an important role in the development of these complications. It is has been reported that NHE is involved in monocytes-macrophages' stimulation. The aim of the present study was to investigate if insulin and glucose can influence NHE activity in human monocytes.

METHODS

Monocytes were isolated from two healthy adults using differential gradient centrifugation and adhesion in gelatin substrate. Intracellular pH was controlled in fluorometer, after cells being charged with BCECF, a specific fluorescent re agent for intracellular measurements of pH. Fluo rescence measurements were changed into pH values with the assistance of a calibration curve which was constructed with the same reagen and with the ionofore nigerisin. Sodium uptake was estimated with ^{22}Na.

RESULTS AND CONCLUSIONS

The results show that monocytes' NHE is stimulated by insulin and high concentrations o glucose. Moreover, we aim to examine if the inhi bition of the NHE influences functions of the monocytes that are related to arteriosclerosis development, e.g. monocyte-macrophage stimu lation, adhesion and migration on extracellula matrix molecules. The long term goal of our re search is to propose the use of inhibitors of NHE in order to protect high risk individuals from dia betes complications and arteriosclerosis.