UP-REGULATION OF RENAL Na⁺, K⁺-ATPase: THE POSSIBLE NOVEL MECHANISM OF LEPTIN-INDUCED HYPERTENSION

Jerzy Bełtowski, Anna Jamroz-Wiśniewska, Ewelina Borkowska, Grażyna Wojcicka

Department of Pathophysiology, Medical University, Łuczynskiego 8, PL 20-000 Lublin, Poland


Hyperleptinemia may be involved in the pathogenesis of obesity-associated hypertension, however, the mechanism of hypertensive effect of leptin has not been elucidated. We investigated the effect of experimental hyperleptinemia on renal function, renal Na⁺, K⁺-ATPase and ouabain-sensitive H⁺, K⁺-ATPase activities in the rat. Leptin administered for 7 days (0.25 mg/kg twice daily sc) decreased food intake on 6th and 7th day of treatment but had no effect on body weight. Systolic blood pressure was 30.5% higher in leptin-treated animals. Urinary excretion of sodium decreased by 35.0% following leptin treatment. Leptin had no effect on potassium and phosphate excretion as well as on creatinine clearance. The activity of Na⁺, K⁺-ATPase in the renal cortex and medulla was higher in leptin-treated rats by 32.4% and 84.2%, respectively. In contrast, leptin had no effect on either cortical or medullary ouabain-sensitive H⁺, K⁺-ATPase. In pair-fed group, in which food intake was reduced to the level observed in leptin-treated group, no changes in sodium metabolism and renal Na⁺, K⁺-ATPase were observed. Leptin decreased urinary excretion of nitric oxide metabolites by 55.0% and urinary excretion of cGMP by 26.3%. Plasma concentration of atrial natriuretic peptide tended to be higher and urinary excretion of urodiilatin was 64.9% higher in leptin-treated animals. These data suggest that hyperleptinemia decreases natriuresis by up-regulating Na⁺, K⁺-ATPase and stimulating tubular sodium reabsorption. This effect is mediated, at least in part, by deficiency of nitric oxide (NO). Abnormal renal sodium retention and vasoconstriction associated with NO deficiency may contribute to leptin-induced hypertension and to blood pressure elevation in hypertensive obese individuals.

Key words: leptin, arterial hypertension, natriuresis, Na⁺, K⁺-ATPase, nitric oxide, atrial natriuretic peptide

# correspondence: e-mail: putflz@askлепios.am.lublin.pl