Antioxidant treatment normalizes renal Na\(^+\),K\(^+\)-ATPase activity in leptin-treated rats

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Abstract:
Hyperleptinemia may be involved in the pathogenesis of obesity-associated hypertension, however, the mechanism of hypertensive effect of leptin is incompletely elucidated. Previously, we have demonstrated that chronic hyperleptinemia causes up-regulation of renal Na\(^+\),K\(^+\)-ATPase and decreases urinary Na\(^+\) excretion. Herein, we investigated whether antioxidant treatment could correct these abnormalities. The study was performed on male Wistar rats. Leptin administered for 7 days (0.25 mg/kg twice daily sc) increased systolic blood pressure by 20.6%. Leptin had no effect on urine output and creatinine clearance but reduced sodium excretion by 40.1%. Na\(^+\),K\(^+\)-ATPase activity in the renal cortex and medulla was higher in leptin-treated rats by 24.3% and 80.6%, respectively. In addition, hyperleptinemia was associated with an increase in plasma and urinary 8-isoprostanes and reduced urinary excretion of nitric oxide (NO) metabolites and cGMP. Co-treatment with a superoxide dismutase mimetic, tempol, or an NAD(P)H oxidase inhibitor, apocynin (2 mM in the drinking water), prevented leptin-induced blood pressure elevation, normalized plasma and urinary 8-isoprostanes, urinary excretion of sodium, NO metabolites and cGMP, as well as prevented up-regulation of renal Na\(^+\),K\(^+\)-ATPase activity. These data suggest that hyperleptinemia increases renal Na\(^+\),K\(^+\)-ATPase activity and reduces natriuresis by inducing oxidative stress-dependent NO deficiency. Antioxidant treatment is effective in leptin-induced hypertension and should be considered in controlling blood pressure in hyperleptinemic obese individuals.

Key words:
leptin, arterial hypertension, natriuresis, Na\(^+\),K\(^+\)-ATPase, nitric oxide, oxidative stress, antioxidants, NAD(P)H oxidase