Apelin receptor expression in ischemic and non-ischemic kidneys and cardiovascular responses to apelin in chronic two-kidney-one-clip hypertension in rats.

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Abstract

BACKGROUND:
Chronic kidney diseases lead to severe cardiovascular consequences such as hypertension and cardiac failure. Apelin, along with its receptor APJ have been shown to involve in cardiovascular functions including blood pressure (BP) lowering effect and also a positive inotropic effect on failing hearts. Therefore we investigated the effect of apelin on BP and cardiac contractility in chronic two-kidney-one-clip (2K1C) hypertension, a kidney disease hypertension model. The changes in the level of apelin and some other hemodynamically effective hormones in serum and apelin receptor gene expression in nonischemic and ischemic kidneys were also assessed.

METHODS:
2K1C was produced by placing a Plexiglas clip around the left renal artery. 16 weeks later, BP and cardiac indices of contractility were measured by power lab system. The mRNA and protein level of APJ were determined by RT-PCR and Western blot methods respectively.

RESULTS:
2K1C increased BP from 115/75 mmHg in sham to 180/120 mmHg in test group. Hypertensive rats had about ten times higher basal left ventricular end-diastolic pressure (LVEDP) (P<0.001) and higher basal LV systolic pressure (LVSP) (P<0.01). Apelin-13 (20 μg/kg, iv) significantly decreased LVEDP and LVSP (P<0.001). Furthermore, apelin in 20 μg/kg dose significantly decreased systolic (SBP) and diastolic (DBP) blood pressures in hypertensive rats. This reduction was persistent and prominent in 40 μg/kg dose. 20 μg/kg apelin increased +LVdp/dt max and -LV dp/dt max. However in the dose of 40 μg/kg SBP, DBP, +LVdp/dt max and -LV dp/dt max greatly decreased. All of these effects were completely blocked by apelin antagonist F13A. 2K1C decreased serum apelin (P<0.05), did not change ang II and arginine-vasopressin levels, and slightly increased serum aldosterone. Apelin receptor mRNA and protein expression significantly decreased in both ischemic and non-ischemic kidneys.

CONCLUSION:
Overall, chronic 2K1C rats showed hypertension and signs of cardiac failure. Apelin in medium doses induced antihypertensive and positive myocardial inotropic effects. Reduction of serum apelin and down regulation of apelin receptors in kidneys of hypertensive rats may play a role in pathophysiology of cardiovascular complications.

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