Renalase Deficiency in Heart Failure: A Novel Mechanism Underlying Circulating Norepinephrine Accumulation

Biao XU; Rong GU
Department of Cardiology, Affiliated Drum Tower Hospital, Nanjing University Medical School, Nanjing 210008, China.
Background

Renalase, synthesized and secreted by kidneys, is a novel and soluble monoamine oxidase that can degrade catecholamines in plasma. Xu et al reported that plasma renalase is markedly reduced in chronic renal failure and nephrectomized rats, and renalase-treated animals exhibited a large reduction in blood pressure accompanied by a decreased concentration of circulating catecholamines. However, until now, it is unclear whether renalse is involved in sympathetic overactivity and catecholamine accumulation in heart failure.


AIMS & Methods

We hypothesized that reduced blood supply to the kidney, as a result of redistribution of peripheral blood flow in heart failure, causes suppression of renalase synthesis and consequently reduced degradation of circulating catecholamines. The aims of the present study were therefore: (a) to evaluate the influence of renal blood flow on renalase synthesis using a unilateral renal artery stenosis model; (b) to ascertain the relationship between renal perfusion flow and renal metabolism of norepinephrine using an in vitro kidney perfusion model; and (c) to investigate the relationship between the expression and activity of renalase in the kidney and the concentration of plasma norepinephrine in an animal model of myocardial infarction with heart failure.
Results (1)

Protein expression of renalalase diminished in the ischemic compared to the non-ischemic kidney.
Results (2)

Norepinephrine clearance is decreased in the hypoperfused kidney.
Results (3)

The flow velocity of renal artery is obviously lower in the heart failure rats.
Results (4)

Protein expression of renalase is decreased in kidneys from heart failure rats.
Results (5)

Renalase expression increases and subsequently decreases with progression of heart failure
Plasma norepinephrine and renalase concentrations are both increased in heart failure rats.
Renalase expression is reduced in the kidneys of heart failure rats.
Discussion

1. Renal blood flow has an important influence on renalase synthesis by the kidney.

2. Norepinephrine can be degraded directly by the kidney.

3. As blood flow or pressure declined, the rate of clearance of norepinephrine decreased in parallel.

4. Renalase expression increases and subsequently decreases with progression of heart failure.
Discussion

1. Renalase deficiency may represent a novel mechanism underlying catecholamine accumulation in heart failure.

2. It remains to be seen whether renalase replacement may prove to be a promising therapy for heart failure.