TITLE

KIDNEYS PLAY A SIGNIFICANT ROLE IN RENALASE TURNOVER, ANOTHER OR NOVEL UREMIC TOXIN???

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OBJECTIVES

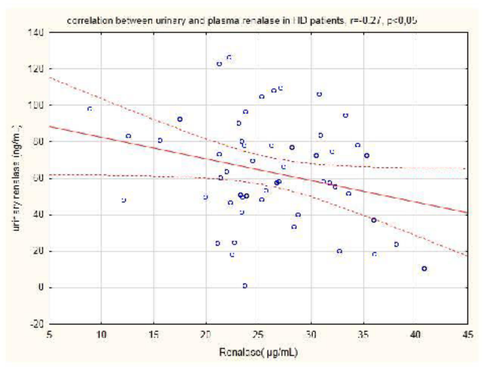
Renalase, a novel substance, may play an important role in the control of blood pressure by its regulatory function of catecholamine metabolism. Renalase could be synthesized not only by the kidney but also by cardiomyocytes, liver and adipose tissue. It probably exerts a hypotensive action, at least in animal models. It has been shown that renalase could be produced by kidneys. Data on renalase levels in serum were conflicting with low activity and high levels reported in patients with hypertension and kidney diseases. There are almost no data available to date on the possible relations between catecholamines and renalase in humans as well as on the presence of renalase in dialysate and ultrafiltrate in dialyzed patients.

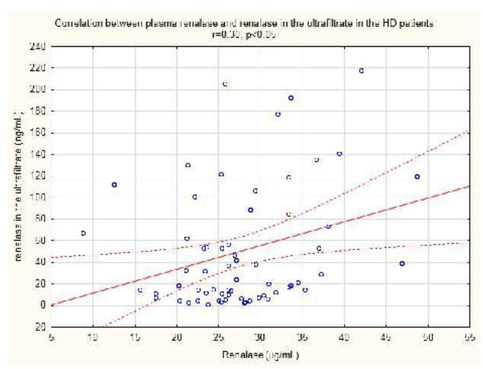
METHODS

Text

The aim of our study was to assess renalase levels in both plasma and urine in healthy volunteers (n=22) as well as in plasma, urine, ultrafiltrate (HD=64) or dialysate (CAPD=14) patients. Renalase (plasma, dialysate/ultrafiltrate, urine), plasma dopamine and noradrenaline were studied using commercially available assays. The enzyme-linked immunosorbent assay (ELISA) kit made by Uscn Life Science Inc. China, using a monoclonal antibody specific to renalase was taken to asses renalase level. The same method was used to assessed catecholamines level - Noradrenaline ELISA kit, Dopamine ELISA kit - both made by Labor Diagnostica Nord GmbH & Co.KG, Germany. Laboratory tests were estimated using standard methods in the central laboratory.

Graphs and tables





RESULTS

Concentration of renalase in urine was significantly lower than in plasma in all groups studied (all $p<0.001$). In addition, renalase in ultrafiltrate/dialysate was lower than in urine. Renalase in both plasma and ultrafiltrate was similar independent of type of dialyzer used (high-flux vs low-flux). Patients with residual renal function had lower renalase relative to anuric patients. In univariate analysis, plasma renalase correlated with urinary renalase ($r=-0.27$, $p<0.05$) and renalase in the ultrafiltrate ($r=0.30$, $p<0.05$) in HD patients and with urinary renalase in healthy volunteers ($r=0.61$, $p<0.01$). Urinary renalase correlated with residual renal function ($r=0.27$, $p<0.05$). Dopamine correlated with renalase in HD population. No correlation between dopamine, norepinephrine, renalase and blood pressure was found. To investigate further the effect of residual renal function on renalase levels we performed Western blot analysis. We selected HD patients after bilateral nephrectomy, unilateral nephrectomy. We selected also controls: hemodialyzed patients with two native kidneys left, subjects after unilateral nephrectomy with normal kidney function and healthy volunteers. We found that patients after bilateral nephrectomy had the highest renalase, followed by unilateral nephrectomy.

CONCLUSIONS

Concluding, apparently kidneys play a role in renalase excretion As yet, we do not know whether renalase is a causative factor or just an innocent bystander in blood pressure control. Regardless of the therapeutic potential and safety of renalase administration, this is a very novel, intriguing protein with poorly defined biochemical functions. Proofs of concept studies are necessary to gather evidence of the pathophysiological link between the kidney, sympathetic tone, blood pressure, and cardiovascular complications

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