Relation of donor kidney injury biomarkers with a 1-year allograft function

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Abstract

Biomarkers in kidney donor's urine and serum may help to predict recipient's graft outcomes. The aim of our study was to evaluate relation of donor's ischemic injury biomarkers with recipient's graft function during first year after kidney transplantation.

Prospective observational study enrolled 29 kidney donors and 48 corresponding recipients who underwent kidney transplantation between May2017 and December2019 at the Hospital of Lithuanian University of Health Sciences. The kidney donor's neutrophil gelatinase–associated lipocalin (NGAL), interleukin-18 (IL-18) in serum and urine and kidney injury molecule-1 (KIM-1) in urine were tested, and relation with recipient's estimated glomerular filtration rate (eGFR) 1, 3, 6, and 12 months after transplantation were evaluated. No significant correlation between studied biomarkers and kidney function at 1 and 3 months after transplantation was found. Only donor's serum NGAL of all biomarkers correlated with eGFR at 6 months ($r=0.31$; $p=0.043$) and at 1 year ($r=0.323$; $p=0.042$). In recipients with eGFR ≥ 45 mL/min/1.73 m^2 1 year after transplantation NGAL in donor's serum (median 61317.0 pg/mL; 23460.7–119700.0) was significantly higher than in recipients with eGFR < 45 mL/min/1.73 m^2 (median 26967.7 pg/mL; 8556.4–46.897) ($p=0.042$). This is an unusual finding as higher concentration of NGAL in donor's serum may indicate more severe donor's acute kidney injury. NGAL in donor's serum correlated with donor's creatinine before transplantation ($r=0.33$; $p=0.023$), but donor's creatinine did not correlate with recipient's kidney function during first year after transplantation. In summary, donor's serum NGAL is related to recipient's kidney function 6 and 12 months after transplantation.

Targeting endogenous cardiotonic steroids for novel therapies

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Abstract

Endogenous cardiotonic steroids (CTS), i.e., Na/K-ATPase (NKA) inhibitors were considered in the regulation of renal sodium transport and arterial pressure. CTS was implicated in fibrosis and pathogenesis of chronic kidney disease (CKD), and preeclampsia (PE). We demonstrated that marinobufagenin (MBG) induces fibrosis via a mechanism involving Fli1, a negative regulator of collagen type-1 synthesis, and MBG-sensitive NKA inhibition is reversed by mineralocorticoid antagonists.

CKD and PE were associated with higher plasma MBG levels, with a four-fold decrease in Fli1 level and a three-fold increase in collagen-1 level in the PE umbilical arteries vs. those from the normal subjects ($p<0.01$). Isolated rings of arteries from the subjects with PE and rats with CKD exhibited impaired responses to the relaxant effect of sodium nitroprusside vs. control vessels. The effects of CKD and PE on Fli1 and collagen type-1 were blocked by the in vitro treatment of umbilical arteries with 10 μmol/L canrenone. Recent data in CKD patients show that higher MBG levels are implicated in vascular fibrosis and that mineralocorticoid antagonists could block this. Our ongoing study tests the hypothesis that CKD patients receiving spironolactone have lower MBG levels.

Several therapeutic strategies for antagonism of the effects of CTS could be offered. Immunoneutralization of heightened levels with anti-MBG antibodies and DigiFab holds promise for the treatment of PE and CKD. Aldosterone antagonists reduce CTS binding to the NKA and alleviate hypertension and fibrosis in CKD.

In conclusion, CTS represents potential therapeutic targets in hypertension and chronic kidney disease.

The SGLT2 inhibitor empagliflozin aggravate urinary tract infection with uropathogenic *Escherichia coli* by a glucose independent mechanism

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Abstract

Patients with diabetes mellitus are more prone to contract urinary tract infections (UTIs). This susceptibility is presumed secondary to urinary glucose accelerating bacterial growth. Here, we test the effect of urinary glucose on growth of uropathogenic *E. coli* in vitro and in a murine model of pyelonephritis.