ISSN 0931-0509 (Print) ISSN 1460-2385 (Online)
Volume 38 Supplement 1 June 2023

ERA
LEADING EUROPEAN NEPHROLOGY

ndt
NEPHROLOGY DIALYSIS TRANSPLANTATION

AN INTERNATIONAL BASIC SCIENCE AND CLINICAL RENAL JOURNAL

60th ERA Congress, 15–18 June 2023

Congress Abstracts

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OXFORD
UNIVERSITY PRESS

#4154

CIRCULATING BETA-TRACE PROTEIN VERSUS CREATININE AS MARKERS OF EARLY KIDNEY (DYS)FUNCTION IN THE NX-INDUCED RAT MODEL OF CHRONIC KIDNEY DISEASE

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Background and Aims: Beta trace protein (BTP) is a low molecular weight protein that has been proposed as an earlier biomarker of decreased

glomerular filtration rate (GFR) and renal damage, than the traditional biomarkers, particularly in the creatinine blind range. Early biomarkers of renal (dys)function are needed to allow, in due time, the detection and treatment, to prevent worsening of the disease. To the authors' knowledge, neither urine nor serum BTP has been assessed in animals with kidney disease. In the present study, we aimed to concomitantly evaluate BTP and creatinine circulating levels, to compare their value as early biomarkers of renal dysfunction, by performing the studies in rat models of mild and moderate chronic renal failure (CRF) induced by nephrectomy.

Method: Male Wistar rats, 12 weeks old, were randomly divided in three groups: Sham ($n = 8$, subjected to surgical process without kidney mass reduction), Mild CRF ($n = 8$, subjected to 1/2 nephrectomy), and Moderate CRF ($n = 7$, subjected to 5/6 nephrectomy). After five weeks, rats were sacrificed, blood and kidneys were collected. We analysed the circulating levels of BTP and creatinine and studied the association of BTP concentration with the glomerular and tubulointerstitial lesions, and with the traditional biomarkers of renal (dys)function, eGFR and creatinine.

Results: The serum levels of BTP were correlated with serum levels of creatinine ($r = 0.575$, $p = 0.004$) and also with eGFR ($r = -0.453$, $p = 0.030$); additionally, we found positive correlations with the total score of mild and advanced tubular lesions ($r = 0.610$, $p = 0.02$ and $r = 0.517$, $p = 0.011$, respectively), observed in kidney sections. The circulating levels of BTP increased with disease severity; Mild CRF showed a higher value of BTP than Sham group, although without statistical significance that was reached in Moderate CRF group, as observed for serum creatinine. The combined use of BTP and creatinine did not improve the discriminatory power in early disease detection. Though, the combination showed stronger correlations with the total score of tubular lesions ($r = 0.849$, $p < 0.001$ for mild tubular lesions and $r = 0.774$, $p < 0.01$ for advanced tubular lesions).

Conclusion: In rat models of mild and moderate CRF induced by nephrectomy, serum BTP levels increased with kidney function worsening, and correlated with disease severity, assessed by GFR and the degree of histopathological alterations. However, the earlier diagnostic value of BTP does not outperform serum creatinine in this model.