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Potential Diagnosis and Prognosis of Urinary Exosomes in Acute Kidney Injury Following Snakebite Envenomation

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BACKGROUND/OBJECTIVES: Acute Kidney Injury (AKI) is an important systemic complication of snakebite and could lead to chronic kidney disease or death. There are not available renal biomarkers for predicting early diagnosis, recovery and prognosis after snakebite. Urinary exosome is a potential tool for reaching these goals.

METHODS: Urinary and blood samples of 13 patients admitted to a reference Center on Toxicological Assistance, Fortaleza-CE, Brazil, after snakebite were assessed in a prospective cohort study in Northeast Brazil. Serpents belonged to Viperidae family. AKI was defined according to KDIGO criteria. AKI group, No-AKI, with albuminuria (Alb+) or without (Alb-) were compared using ANOVA-one way in GraphPad Prism v.8 (GraphPad Software, San Diego, CA, USA). Urinary protein levels were determined by western blot of isolated exosomes in patients with and without renal alterations and healthy volunteers. Tubular transporters (AQP2: aquaporin-2; NKCC2: Na-K-2Cl cotransporter) and a glomerular protein (Nephrin) were evaluated. Bands were quantified by densitometry analyses using imageLab software.

RESULTS/CONCLUSIONS: Healthy control (n=6), No-AKI/Alb- (n=4), No-AKI/Alb+ (n=2) and AKI/Alb- (n=2) were significantly different according to urinary expression of NKCC2 ($P<0.0001$), Nephrin ($P=0.004$) and AQP2 ($P=0.01$). The No-AKI/Alb+ group presented higher expression of NKCC2 than No-AKI/Alb- group, however lower than AKI/Alb- group. Other patients were excluded by methodologic limitations (n=5). The expression of glomerular and tubular proteins in No-AKI/Alb+ and AKI/Alb- groups proposed glomerular and tubular mechanisms of AKI induced by snake venoms. This study pointed out albuminuria as an early biomarker for AKI following Viperidae snakebite. The NKCC2 transporter became higher significant level than AQP2 and Nephrin, suggesting tubular damage as an important pathway of AKI pathogenesis. NKCC2 in urinary exosomes is a potential new biomarker for validation in AKI due to snakebites. Further studies need to analyze the correlation between exosomes and albuminuria in larger number of patients.