PAI-1: A NEW URINARY MARKER OF ACUTE KIDNEY INJURY INDUCED BY GENTAMICIN, ISCHEMIC-REPERFUSION AND SEPSIS PROCEDURES.

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Introduction

Acute Kidney Injury (AKI) is understood as a clinical syndrome, secondary to multiple etiologies, characterized by an abrupt deterioration in renal function. It is a relevant health problem, since it presents a high morbi-mortality with very important human and social consequences. It is estimated that approximately 1 to 7% of patients admitted to hospitals have this syndrome. The mortality rate associated with AKI is around 45% and, since a large number of cases develop in the ICU, a marked increase can be found up to 80% in the state of one multiorgan failure. A critical aspect for the optimal clinical handling of AKI is an early diagnosis. Important progress has been made in the last decade towards an increasingly earlier detection based on novel and more sensitive urinary markers. However, AKI diagnosis may still be improved in an individual-drug basis, for enhanced theranostics and a more individualized medicine.

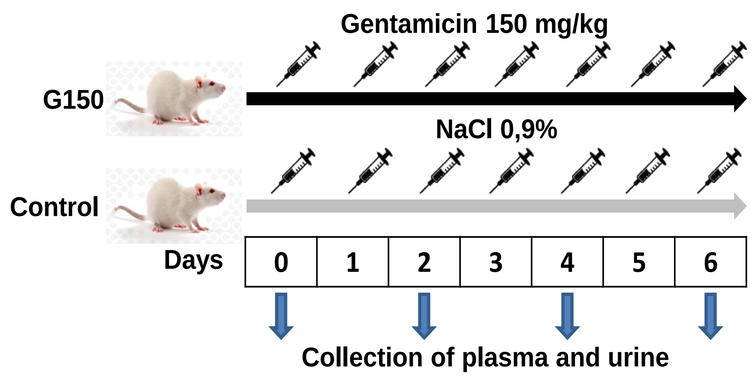
Aims

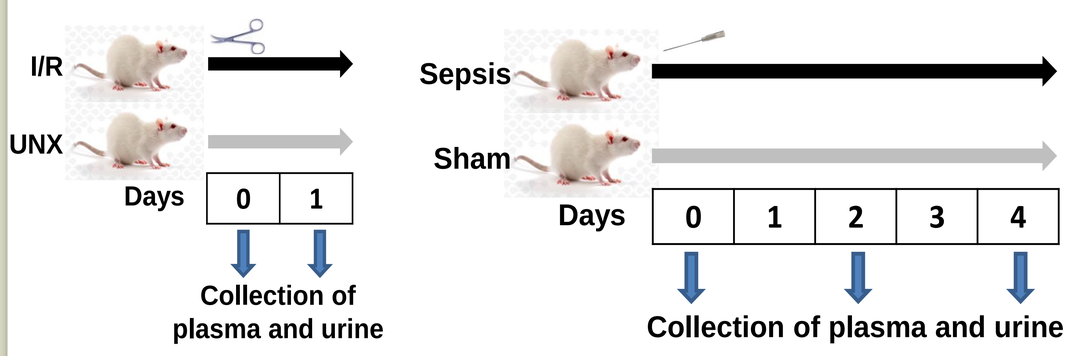
We decided to study the plasminogen activator inhibitor-1 (PAI-1) as potentially urinary marker of gentamicin, ischemic-reperfusion and sepsis procedures.

Methods / experimental design

Male Wistar rats were administrated by a daily dose of gentamicin (150 mg/kg) or not, animals underwent one hour of warm renal ischemia or not, and animals underwent cecal ligation and 4 punctures to induce sepsis or not.

Renal function was monitored by means of plasma creatinine, creatinine clearance and plasma urea. Renal morphology and tissue integrity were assessed by histological studies and urinary PAI-1 was determinate by Western blot.





Conclusions

PAI-1 is a potentially urinary marker of gentamicin´s nephrotoxicity, ischemic-reperfusion and sepsis procedure. It will be help to better delineate the pharmaco-toxicological profile of gentamicin and to improve its clinical utility. In addition, PAI-1 will help to diagnose AKI in septic patients and in those who have suffered an ischemic process.

Results

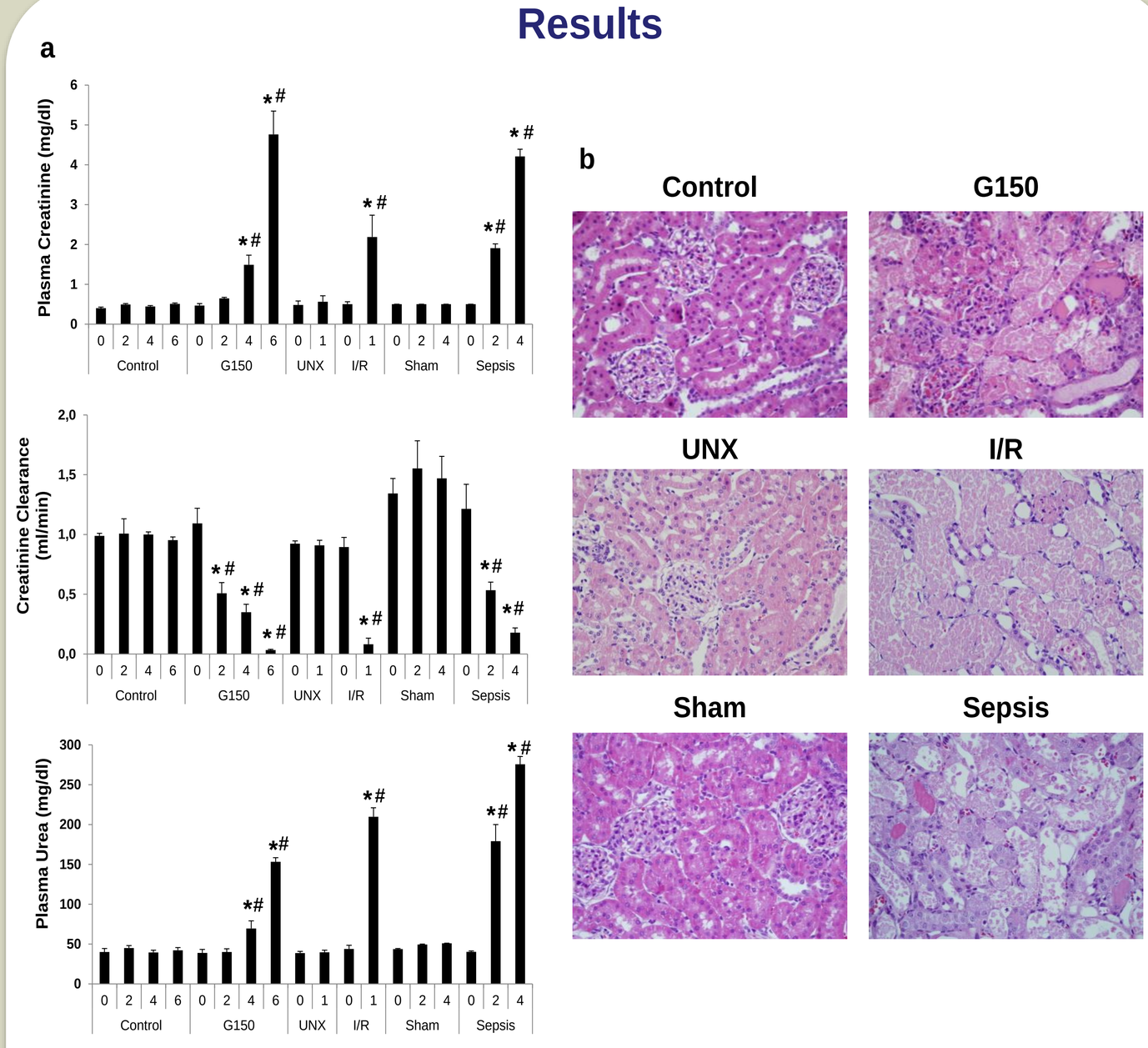


Fig 1. Plasma creatinine concentration, creatinine clearance and plasma urea concentration (a) and representative images of renal tissue sections stained with Hematoxilin&Eosin at the maximum renal damage (b) in control rats (Control; n=5), rats treated with gentamicin 150 mg/kg/day (G150; n=5), rats with 60 minutes of renal ischemia (I/R; n=5) or with a contralateral uninephrectomy (UNX; n=5) and rats underwent cecal ligation with 4 punctures (Sepsis; n=5) or not (Sham; n=5). Statistically significant: *z>1,96 vs. control group (for G150), vs. UNX group (for I/R) or vs. Sham group (for Sepsis) same day; #: z>1,96 vs. day 0 in the same group.

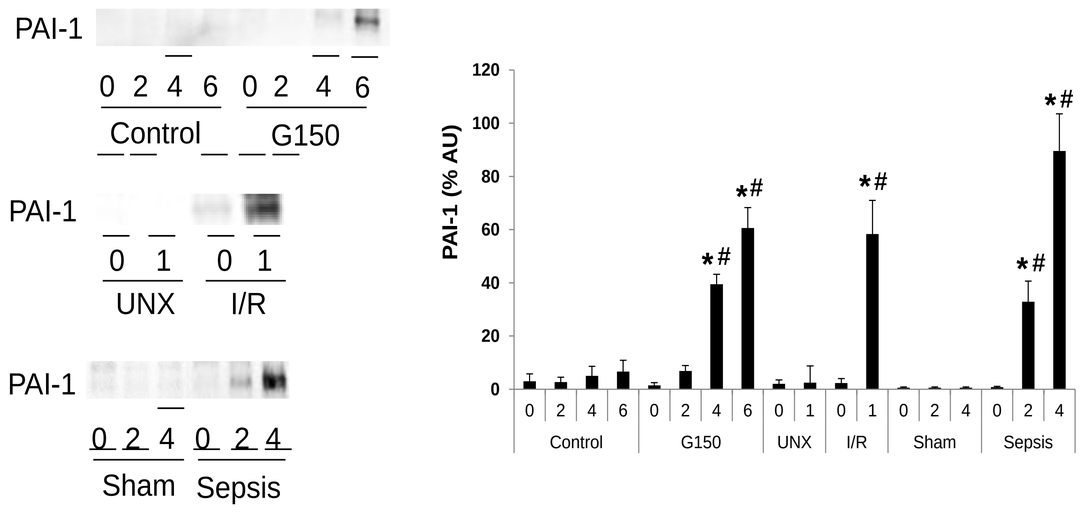


Fig 2. Evolution of urinary PAI-1 excretion determined by western blot. Values are expressed as mean ± SEM (n=5). Statistically significant: *z>1,96 vs. control group (for G150), vs. UNX group (for I/R) or vs. Sham group (for Sepsis) same day; #: z>1,96 vs. day 0 in the same group.

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