Propeptide of procollagen type i as a new marker associated to early diagnosis of acute kidney injury induced by gentamicin.

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Introduction

Acute kidney injury (AKI) occurs in response to certain drugs, metals and a variety of other insults, however, AKI is nowadays diagnosed when the patient presents evident alterations of renal excretory, which show clinically detectable signs and symptoms (e.g. increased serum creatinine, proteinuria, etc.), at this a point, the damage is very extensive and the treatment very difficult. A key aspect for the clinical handling of AKI is an early diagnosis. Gentamicin is an aminoglycoside antibiotic widely used for the treatment of many infectious diseases. Collagen metabolism has been linked to epithelial damage and repair. Accordingly, serum levels of metabolites from collagen I have been proposed to mark, in addition to bone disorders, other diseases coursing with tissue damage.

Aims

The aim of this work is studying the relation between urinary excretion of the procollagen I carboxyterminal telepeptide (PIP), a subproduct of collagen turnover, and the degree of renal damage caused by gentamicin.

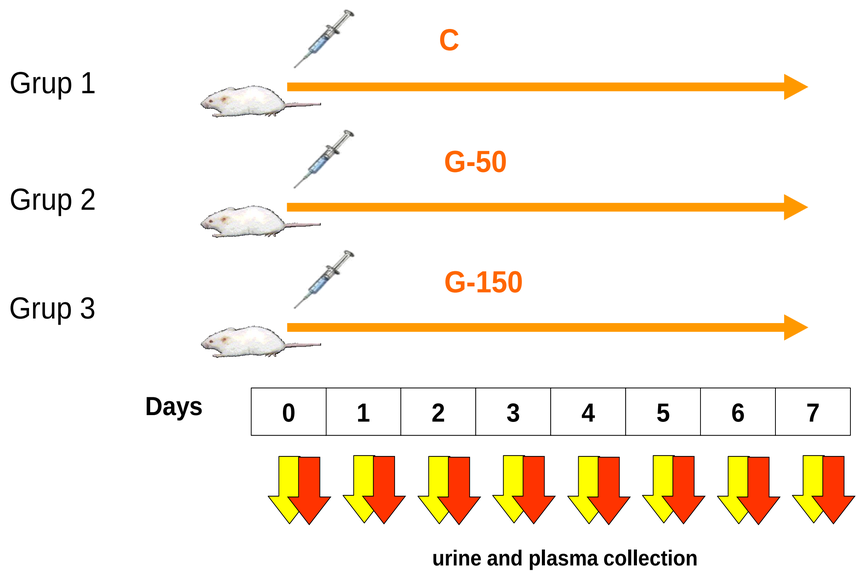
Methods/ experimental design

- Experimental Groups (female Wistar rats weighing 190-220 g):
  - Group 1: daily saline (C) i.p. (day 0-6)
  - Group 2: daily 50 mg/kg body weight Gentamicin (G-50) i.p. (day 0-6)
  - Group 3: daily 150 mg/kg body weight Gentamicin (G-150) i.p. (day 0-6).

-Renal toxicity was evaluated by measuring plasma creatinine, urine proteins and N-acetyl-glucosaminidase (NAG). Renal morphology and tissue integrity were assessed by histological studies.

-ELISA and Western blot were used to investigate the presence of new urine markers.

Schematic representation of the experimental design



Conclusions

Our results indicate that the increased urinary levels of PIP correlate with low dose Gentamicin regime, which hoards a potential for the diagnosis of clinically relevant, subclinical renal conditions induced by this aminoglycoside antibiotic. It also suggests that collagen metabolism and turnover is involved in gentamicin-induced AKI.

Results

Characterization of the renal function at day 6

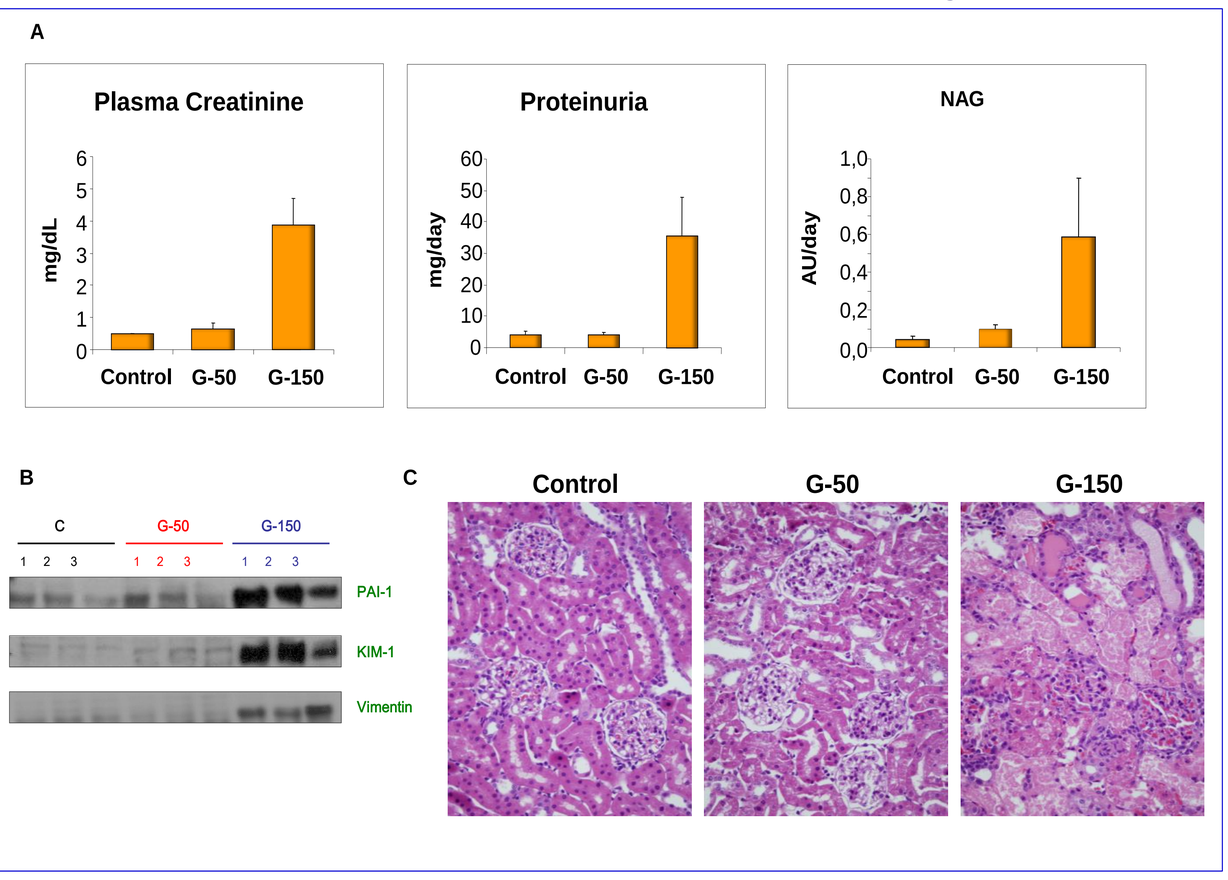


Figure 1. Classical diagnostic markers of nephrotoxicity measured in urine from rats treated during 7 days with 0 (Control), 50 (G-50) or 150 (G-150) mg/day gentamacin (per Kg of body weight). (A) Graphs represent determinations of plasma creatinine, urine protein daily excretion and daily urine activity of N-acetyl-glusoaminidase (NAG) after 7 days of treatment. (B) Representative images of Western blot analysis of PAI-1, KIM-1 and vimentin levels in renal tissue homogenates from 3 randomly selected animals from C, G-50 and G-150 groups. Representative images (400X) of the cortex of hematoxilin–eosin-stained renal sections from C, G-50, and G-150 rats (n=3) (C)

New urine markers associated to gentamicin nephrotoxicity

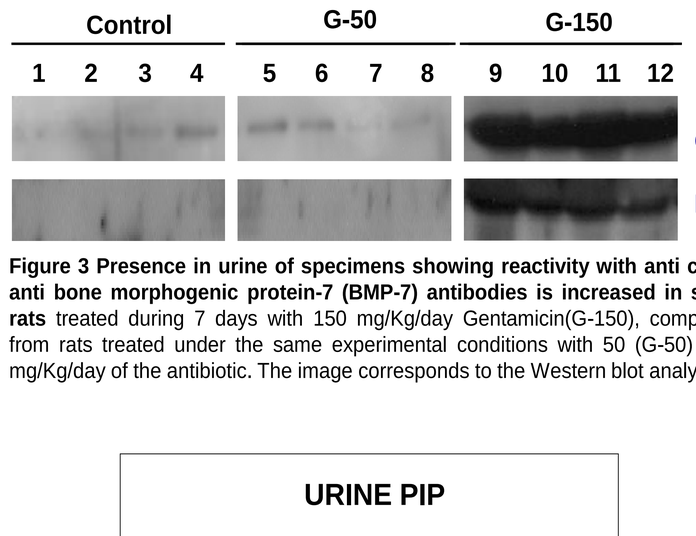


Figure 3 Presence in urine of specimens showing reactivity with anti collagen I and anti bone morphogenic protein-7 (BMP-7) antibodies is increased in samples from rats treated during 7 days with 150 mg/Kg/day Gentamicin(G-150), compared to those from rats treated under the same experimental conditions with 50 (G-50) or 0 (control) mg/Kg/day of the antibiotic. The image corresponds to the Western blot analysis.

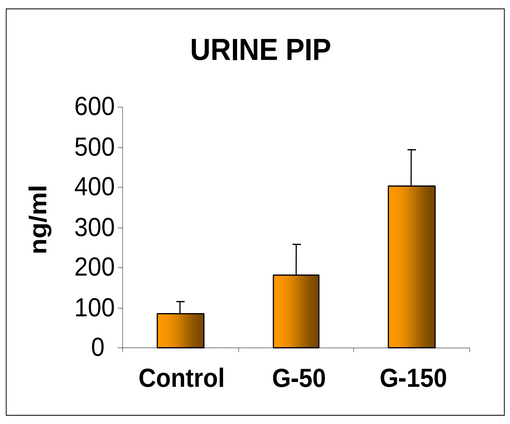
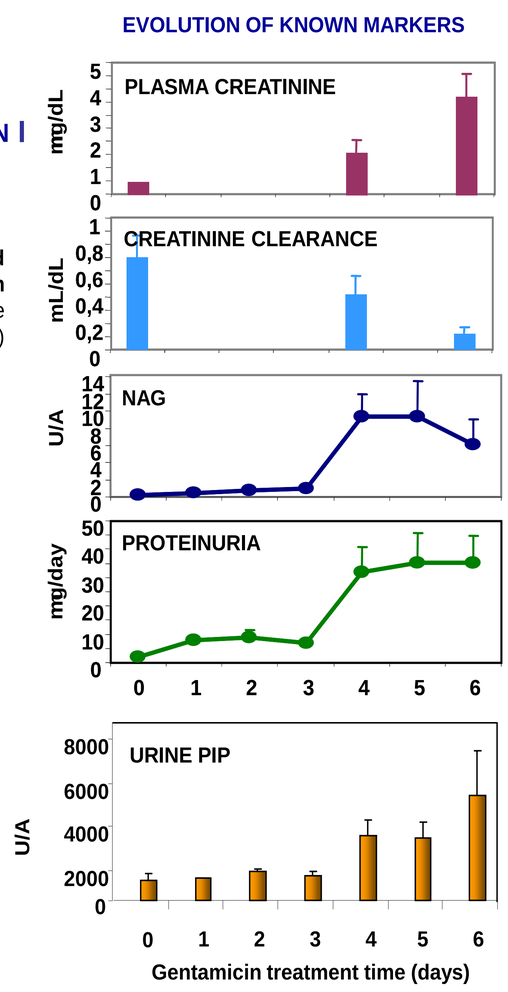


Figure 2. Urine concentration of carboxy-terminal propeptide of procollagen type I (PIP) increases in gentamicin-treated rats. PIP was determined by ELISA in urine from rats treated during 7 days with 0 (control, n=6), 50 (G-50, n=6) or 150 (G-150, n=5) mg/Kg/day Gentamicin.



Supported by the Kidney Research Network REDINREN of the Instituto de Salud Carlos III (ISCIII), Spain, co-funded by FEDER