MICROSOMAL AND EXOSOMAL GLUTAMYL AMINOPEPTIDASE IN URINE ARE EARLY AND PREDICTIVE BIOMARKERS OF RENAL DYSFUNCTION IN CISPLATIN-TREATED RATS

De Gracia MC[1], Montoro-Molina S[2], Quesada A[1], Osuna A[1], O'Valle F[3], Gómez-Guzmán M[2], Vargas F[4], Wangensteen R[2].

[1]Unidad de Nefrología, FIBAO, Hospital Virgen de las Nieves, Granada. [2]Área de Fisiología, Departamento de Ciencias de la Salud, Universidad de Jaén. [3]Departamento de Anatomía Patológica, IBIMER, Universidad de Granada. [4]Departamento de Fisiología, Facultad de Medicina, Universidad de Granada

OBJECTIVES

In previous studies we have demonstrated that glutamyl aminopeptidase (GluAp) is an early and predictive biomarker of renal dysfunction in cisplatin-treated rats, an experimental model of acute kidney injury. The aim of this work is to study if the measurement of GluAp in microsomal and exosomal fractions of urine can improve the early diagnosis of renal dysfunction in this model.

METHODS

Urine samples from control and cisplatin-treated rats (n=10 each group) were collected 24 hours after injection of cisplatin and subjected to differential centrifugation at 17.000 and 200.000 g in order to obtain microsomal and exosomal fractions, respectively. GluAp was measured by ELISA in the different fractions.

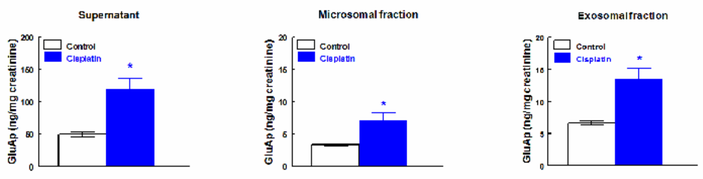

Figure 1. GluAp excretion in supernatant, microsomal and exosomal fraction of urine samples from Control and Cisplatin groups collected 24 hours after injection. Data are expressed in ng/mg creatinine. Data are expressed as mean ± SEM; * p<0.01 Cisplatin vs. Control (n=10 each group).

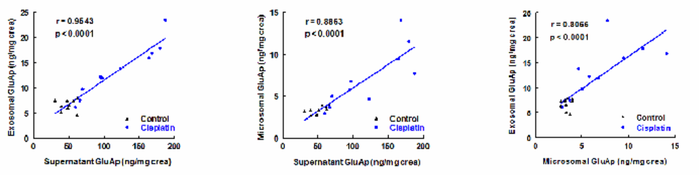

Figure 2. Linear regressions between GluAp excretion (ng/mg creatinine) in supernatant and exosomal fraction (left), supernatant and microsomal fraction (middle), and microsomal and exosomal fractions (right) of urine samples collected 24 hours after injection.

RESULTS

In cisplatin-treated group, GluAp was increased in microsomal and exosomal fractions of urine per mg of creatinine (Fig. 1), per mg of protein content in each fraction and per weight of rat and day.

GluAp content in the different fractions was correlated (Fig. 2), and exosomal fraction was the richest fraction for this enzyme. GluAp excreted in exosomal fraction per mg of creatinine was highly correlated (r=0.7587; p=0.0001) with serum creatinine (SCr) concentration at the end of the experiment, and it was the best biomarker to distinguish rats that developed concentrations of SCr ≥ 0.61 (Table 1).

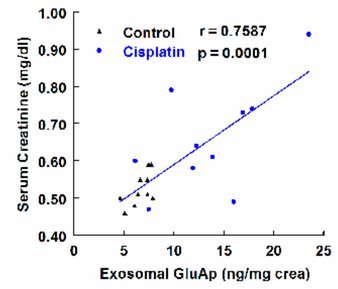

Figure 3. Linear regression between GluAp excretion (ng/mg creatinine) in exosomal fraction of urine samples collected 24 hours after injection with SCr concentration determined at the end of the experiment.

Table 1. ROC-AUC and sensitivity at 95 % of specificity for GluAp measured in supernatant, microsomal and exosomal fractions of urine collected 24 hours after cisplatin injection to distinguish animals with SCr ≥ 0.61 at the end of the experiment.

	AUC	Sensititivity (%)
Exosomal GluAp (ng/mg Cr)	0.9562	70.6
Supernatant GluAp (ng/mg Cr)	0.9478	63.6
Microsomal GluAp (ng/mg Cr)	0.9340	45.2

CONCLUSIONS

We conclude that microsomal and exosomal GluAp are early and predictive biomarkers of renal dysfunction. Measurement of GluAp in these fractions supposes an improvement in the early diagnosis of this alteration in cisplatin-treated rats. Urine fractionation might be a useful tool in the search of biomarkers for different renal pathologies.

GOBIERNO DE ESPAÑA · MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD · Instituto de Salud Carlos III
Unión Europea · Fondo Europeo de Desarrollo Regional
"Una manera de hacer Europa"

HOSPITAL UNIVERSITARIO Virgen de las Nieves

FIBAO FUNDACIÓN PÚBLICA ANDALUZA PARA LA INVESTIGACIÓN BIOSANITARIA DE ANDALUCÍA ORIENTAL ALEJANDRO OTERO

UNIVERSIDAD DE JAÉN

53 ERA
185--MP
Acute Kidney Injury. Experimental.
maria del
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA AUSTRIA MAY 21-24 2016
PosterSessionOnline.com