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EFFECT OF CT-1 BLOCKADE WITH ANTI-CT-1 ANTIBODIES ON THE SEVERITY OF ACUTE RENAL FAILURE INDUCED BY UNILATERAL RENAL ISCHEMIA

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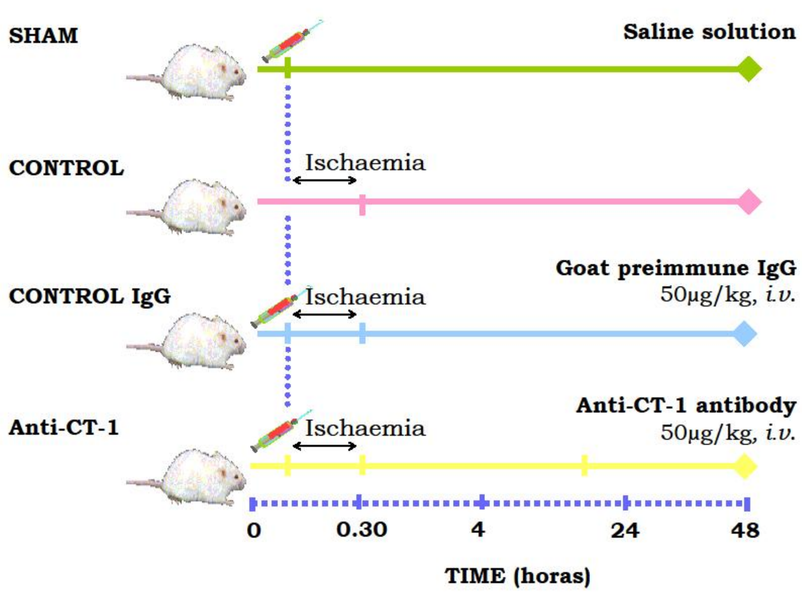
INTRODUCTION

Ischaemia/reperfusion (I/R) injury is a major cause of acute kidney injury and an important determinant of long-term kidney dysfunction. I/R injury is now recognized as a highly complex cascade of events, in which inflammation is known to be a key mediator.

Cardiotrophin-1 (CT-1) is a member of the interleukin 6 (IL-6) family of cytokines, which protects cardiac myocytes and liver from ischemic insults. It has been reported that increased endogenous CT-1 production can act as a protective factor against ischemia. The purpose of this study is to assess the effect of endogenous CT-1 on the severity of acute renal injury induced in a mouse model of unilateral renal ischemia by blocking CT-1 actions with anti-CT-1 antibody.

MATERIALS AND METHODS

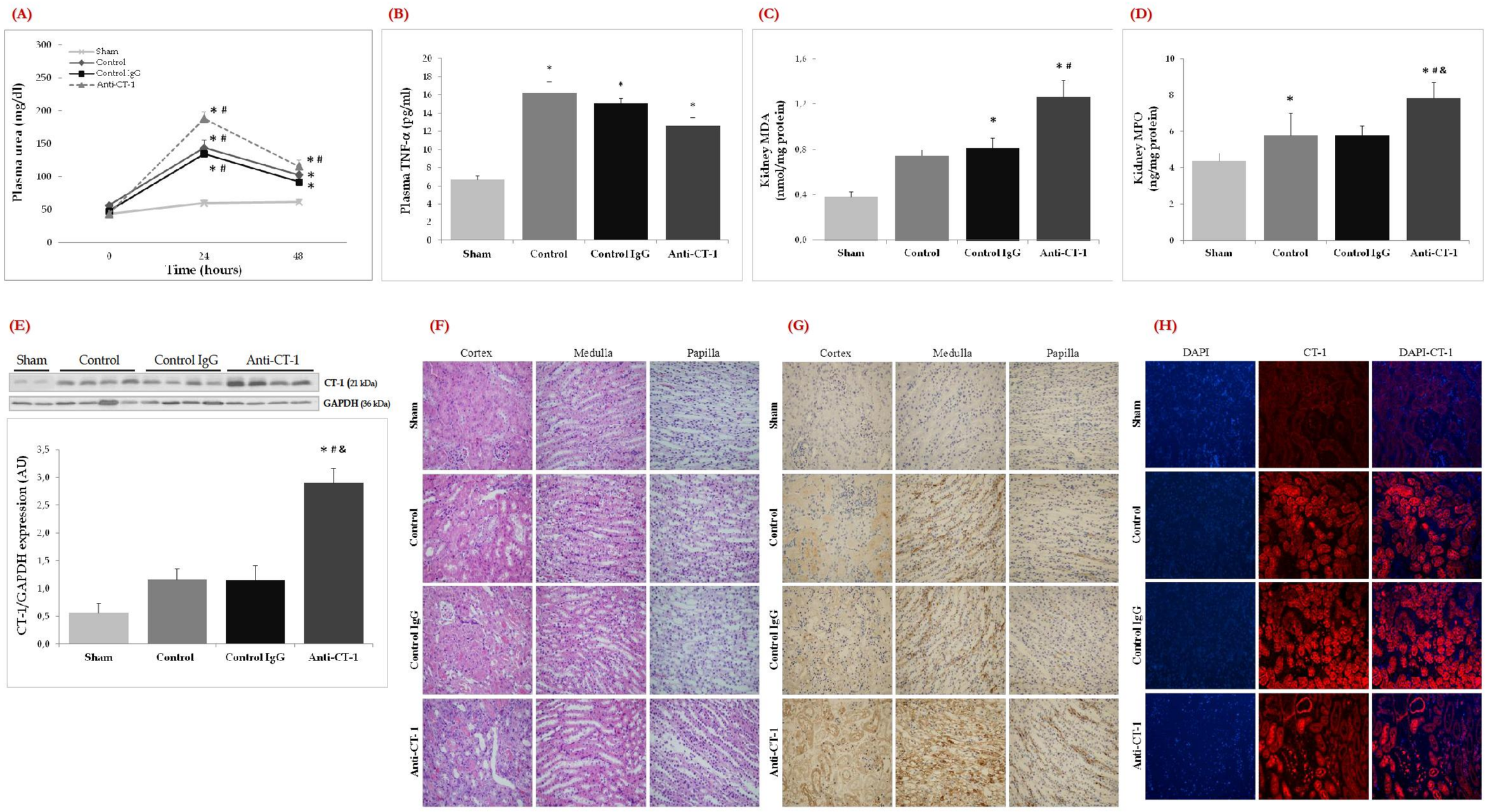


C57BL/6 mice were randomized into eight groups (n: 6-8) Control group, Control IgG group, Anti-CT-1 group and Sham group.

After 30 min left renal ischemia (with contralateral nephrectomy) and 24 or 48 h. reperfusion, mice were sacrificed and blood samples were collected for determination of serum urea, CT-1 and TNF-α levels. Left kidney was excised and homogenized for the analysis of malonyldialdehyde (MDA), myeloperoxidase (MPO) and CT-1, and for histological examination (H&E, CT-1 and ED-1 positive cells).

RESULTS

Effect of anti-CT-1 antibody on plasma and kidney parameters in mice subjected to renal I/R



(A) Plasma urea (mg/dL), (B) plasma tumor necrosis factor-alpha (TNF-α) (pg/mL), (C) kidney malonyldialdehyde (MDA) (nmol/mg protein), (D) kidney myeloperoxidase (MPO) (ng/mg protein) and (E) kidney CT-1 expression in the four experimental groups at 4 hours (B) or 48 hours after surgical operation (A, C, D and E). Data expressed as mean EEM, * $p<0.05$, *vs* Sham; # $p<0.05$, *vs* Control; & $p<0.05$, *vs* Control IgG.

(F) Sections of kidney stained with haematoxylin-eosin, (G), CD-68 (ED-1 positive cells) and (H) immunofluorescence staining of CT-1 in the four experimental groups at 48 hours after surgical operation.

CONCLUSIONS

Our study demonstrated that anti-CT-1 antibody administration exaggerated the severity of ischemic kidney injury in mice, possibly as a result of CT-1 blockade. These data reinforce the role of endogenous CT-1 in protecting the kidney from I/R damage.

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