The late inhibition of inhibitor of IkB kinase attenuates acute kidney injury and the subsequent development of fibrosis in a rato del of ischemia/reperfusion injury.

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THE LATE INHIBITION OF INHIBITOR OF IKB KINASE ATTENUATES ACUTE KIDNEY INJURY AND THE SUBSEQUENT DEVELOPMENT OF FIBROSIS IN A RAT MODEL OF ISCHAEMIA REPERFUSION INJURY.

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Abstract

INTRODUCTION: Sepsis is the most common cause of acute kidney injury (AKI), and AKI has now been described as a major risk factor for chronic kidney disease (CKD). Post-inflammatory renal scarring from the activation of nuclear factor-kappaB (NF-kappaB) due to AKI may be an important contributor to CKD development. NF-kappaB is a diverse family of transcription factors activated by inhibitor of kappaB kinase (IKK).

METHODS: Male Wistar rats underwent a right-hand nephrectomy and unilateral renal ischaemia for 30 minutes or sham operation (no ischemia) (n=8). Two groups of animals subject to ischemia reperfusion injury (IRI) were administered the IKK inhibitor IKK16(1mg/kg i.v. in 10% DMSO) given at 24-h post-reperfusion. Control animals were allowed to recover and culled at 1 (n=4), 2 (n=4), 3 (n=4), 7 (n=4), 14 (n=4) or 28 (n=7) days, and IKK16 treated animals were culled at 2 (n=4) or 28-days (n=7). 24-h prior to experiment termination, rats were placed into metabolic cages for urine collection.

RESULTS: When compared to sham-operation rats, rats subjected to unilateral renal IRI (control) developed AKI. Late administration of IKK16 resulted in a significant improvement in renal function (lower creatinine/urea) and structural injury at 48-h post reperfusion. When compared to rats subjected to sham-operation, control rats demonstrated significant increases in Sirius red staining (indicative of fibrosis) at 28-days post reperfusion, which was markedly reduced by the late administration of IKK16.

CONCLUSION: The late inhibition of IKK may, therefore, have therapeutic potential in the recovery of AKI and the prevention of subsequent CKD.

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