Acute Kidney Injury

Incidence and Outcome of Acute Kidney Injury in Hospitalized Patients in a Single Center

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Objective: This study was to determine the incidence and mortality rate of acute kidney injury (AKI) among hospitalized adult patients in a tertiary metropolitan hospital of China, and to evaluate the impact of AKI on 28-day mortality, cost and length of stay (LOS).

Methods: Patients of Zhongshan Hospital, Fudan University, Shanghai between November 3rd, 2014 and November 9th, 2014 were screened by the hospital medical database. The presence and severity of AKI were assessed by the KDIGO criteria. Follow-up biochemical and clinical data were used to determine short-term (28 days) outcomes.

Results: There were 2563 patients during the study period and 92 (3.59%) met the diagnostic criteria of AKI. The median age of AKI patients was 64 years, 70.7% were male, 12% received renal replacement therapy. 23 patients (25%) were community-acquired AKI, the leading cause was nephrotoxic drugs (26.1%), infection (21.7%) and heart failure (17.4%). Hospital-acquired AKI was 75%, the leading cause was surgery (62.7%), infection (14.5%) and nephrotoxic drugs (8.7%). The AKI group had significantly longer LOS than the non AKI group (14 vs. 6 days). The 28d mortality of AKI was 7.6%. Complete, partial and no renal recovery was observed in 28.3%, 23.9% and 21.7% of the patients, respectively. Of AKI patients, AKI stage (KDIGO criteria), malignancy and albumin were independent risk factors of 28-day mortality according to multivariate logistic regression.

Conclusion: AKI is prevalent in the Chinese hospitalized patients. Slight elevations of serum creatinine are associated with significantly increased mortality, LOS and hospital cost. Moreover, outcomes are related directly to the severity of AKI.

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Orphan Nuclear Receptor RORalpha Exerts Protective Potential in Acute Kidney Injury via Transcriptional Activation of HIF-1

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Background: Emerging evidence indicates that retinoid-related orphan receptor alpha (RORalpha), a member of the ROR subfamily of nuclear receptors, mediates key cellular adaptions to hypoxia and contributes to pathophysiology of many disease states. However, the potential renal functions of RORalpha in response to ischemia/reperfusion (I/R) injury remain unclear. Here, we investigated the renal expression and biological function of RORalpha in acute kidney injury (AKI).

Methods: I/R injury was induced by 35 min bilateral clamping of the renal pedicle and 24 h reperfusion in wild-type and staggerer [RORalpha(sg/sg)] mice, a natural mutant strain lacking RORalpha expression. Renal injury and RORalpha abundance were analyzed. In addition, human proximal tubular cell line (HK-2) was used to investigate the expression of RORalpha under hypoxia.

Results: RORalpha was detected in both mouse renal endothelial and tubular epithelial cells. Significant up-regulation of RORalpha was found after renal I/R injury. Compared with wild-type, RORalpha(sg/sg) mice displayed significantly increased levels of serum creatinine (2.30 ± 0.21 vs. 1.18 ± 0.35 mg/dl, p < 0.01), renal tissue damage, and pro-inflammatory cytokine production after ischemic kidney injury (Figure 1). Further mechanistic studies indicated that RORalpha agonists enhanced transcriptional activity of hypoxia-inducible factor 1alpha (HIF-1alpha) in HK-2 cells, which was abolished by siRNA-mediated silencing of endogenous RORalpha.

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Injury in Mice

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Background: Ischemia/reperfusion (IR) is a main cause of acute kidney injury (AKI). Up-regulated caspase-3, a key enzyme involved in inflammation and apoptosis, was revealed in renal IR injury and reversed by a novel cyclic helix B peptide (CHBP), derived from erythropoietin. Here, caspase-3 small interfering RNA (C3siRNA) and/or CHBP were applied in a mouse model to further explore underlying mechanisms.

Methods: Bilateral renal occlusion for 30 min was performed in male C57BL/6 mice and followed by 48 h reperfusion. 0.03 mg/kg CHBP was injected intraperitoneally post reperfusion. Serum and kidney samples were collected for renal function, histology and molecular biology analyses.

Results: Serum creatinine and tubulointerstitial damage (TID) score were increased by IR injury, but reduced by C3siRNA and/or CHBP (all P < 0.01). In addition, the expression of 17 kD active caspase-3, active caspase-3+ cells and apoptotic cells were raised by IR injury, but reduced by C3siRNA and/or CHBP (P < 0.01). More interestingly, there was a significant reduction in TID in the kidneys treated with both C3siRNA and CHBP compared with its sole treatment.

Conclusion: C3siRNA and CHBP ameliorated IR injury, both of which might have certain synergetic effects. CHBP might reduce active caspase-3, subsequently affect apoptosis, and improve renal function and structure.

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