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论著

# 尿中肾损伤分子1水平升高对大鼠早期肾损伤的预测作用

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摘要 目的 评价尿中肾损伤分子1(KIM-1)对大鼠早期肾损伤的预测作用。方法 制备顺铂、庆大霉素和环孢素诱导的大鼠肾损伤模型。顺铂模型大鼠于单次ip给药后第3，5，6和7天，庆大霉素模型于首次ip给药后第3，7，10和13 天，环孢素模型于首次ig给药后第8，15，36和53天通过腹主动脉取血，分离血清。各组大鼠于处死前24 h收集尿液。用自动生化仪检测血清肌酐（SCr）和血尿素氮（BUN）及尿肌酐（UCr）水平，采用ELISA法检测尿KIM-1水平，HE染色进行肾脏组织病理学检查。结果 与正常对照组相比，顺铂模型大鼠单次给药后第3天肾组织病理改变不明显，而尿KIM-1升高了4.7倍，SCr和 BUN升高了0.3和0.7倍；第5和6天，KIM-1升高了10.0和8.7倍，SCr升高了1.9和3.3倍，BUN升高了3.0和5.1倍，第5天肾组织出现明显的病理改变；第7天，KIM-1水平升高了16.5倍，SCr和 BUN水平略降，为正常对照组的1.2和3.0倍。庆大霉素模型大鼠，与正常对照组比较，于首次给药后第7天，SCr和BUN水平和肾组织未见明显改变，KIM-1水平升高了2.6倍；第10和13天，SCr水平升高了1.7和1.6倍, BUN升高了2.0和1.9倍，KIM-1升高了12.5和33.9倍，第10天肾组织出现明显的病理改变。环孢素模型大鼠，与正常对照组比较，在第8天，SCr和BUN水平和肾组织未见异常，KIM-1升高了正常对照组的0.6倍；第15，36和53天，KIM-1分别升高了1.7，4.3和9.3倍，SCr分别为1.0，1.0和1.2倍，BUN分别升高了0.4，0.6和1.2倍，肾组织在第53天时出现明显的病理改变。顺铂模型组SCr, BUN和KIM-1的受试者操作特性曲线的曲线下面积（AUC）分别为0.934，0.953和0.979，庆大霉素模型组SCr, BUN和KIM-1的AUC分别为0.877，0.713和0.932，环孢素模型组SCr, BUN和KIM-1的AUC分别为0.668，0.766和0.976。结论 在顺铂、庆大霉素和环孢素诱导的肾损伤模型中，尿KIM-1可用于早期肾损伤的预测。

关键词 肾损伤 肾损伤分子1 顺铂 庆大霉素 环孢素

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# Predictability of increasing level of kidney injury molecule-1 in urine for rat early kidney injury

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**Abstract**

OBJECTIVE To evaluate the predictive ability of urine kidney injury molecule-1（KIM-1）for early renal injuries in rats. METHODS The renal injury models of rats were induced by cisplatin, gentamicin and ciclosporine, respectively. Serum samples taken from abdominal aorta were collected on the 3rd, 5th, 6th and 7th day after cisplatin was once ip treated; on the 3rd, 7th,10th and 13th day after gentamicin was first ip treated and on the 8th, 15th, 36th and 53th day after ciclosporine was first ig treated. Urine was collected before necropsy ( 24 h collected period). The levels of serum creatinine (SCr), blood urea nitrogen (BUN) and urine creatinine (UCr) were detected using automatic biochemical analyzer. KIM-1 concentration in urine was analyzed with ELISA. Pathological changes in renal tissue were observed with optical microscope following HE staining. RESULTS In cisplatin treated group, the rat kidney had no observable histomorphological change, but urine KIM-1, SCr and BUN increased by 5.7, 1.3 and 1.7-fold relative to normal control on the 3rd day. KIM-1 increased by 11.0 and 9.7-fold, SCr increased by 2.9 and 4.3-fold, and BUN increased by 4.0 and 6.1-fold on the 5th and 6th days compared with control group. Kidney tissue had remarkable changes on the 5th day compared with control group. KIM-1 increased by 17.6-fold but SCr and BUN only increased by 2.2 and 4.0-fold compared with control group on the 7th day. For gentamicin treated group, SCr, BUN and kidney tissue had no significant change, but KIM-1 increased by 2.6-fold on the 7th day relative to the normal control. SCr, BUN and KIM-1 increased

significantly on the 10th and 13th day compared with control group. They increased by 2.7 and 2.6-fold for SCr, 3.0 and 2.9-fold for BUN and 13.5 and 34.9-fold for KIM-1 compared with control group. Histomorphological changes were observed in renal tissue on the 10th day. For ciclosporin treated group, SCr, BUN and kidney tissue had no significant change, but KIM-1 increased by 1.6-fold on the 8th day. Compared with control group, KIM-1 had increased by 2.7, 5.3, and 10.3 -fold on the 15th ,36th and 53th day, while SCr increased by 2.0, 2.0 and 2.2-fold and BUN increased by 1.4, 1.6 and 2.2-fold. Nephridial tissue had significantly histomorphological changes on the 53th day. When compared with the area under curve (AUC) of the 3 biomarker`s receiver operating characteristic, the AUC of cisplatin were 0.934, 0.953 and 0.979, the AUC of gentamicin were 0.877, 0.713 and 0.932 and the AUC of ciclosporin were 0.688, 0.766 and 0.976. CONCLUSION KIM-1 increases significantly before kidney tissue has slight or observable pathological changes, and KIM-1 is a good predictor for early renal injury.

**Key words** kidney injuries kidney injury molecule-1 cisplatin gentamicin cyclosporine

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