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大鼠肾缺血再灌注损伤后p38丝裂原活化蛋白激酶的活化及氧自由基清除剂对其的影响 点此下载全文

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摘要：

目的：观察肾缺血再灌注损伤后p38活化的情况，并探讨应用氧自由基清除剂tempol后对其的影响。方法：雄性SD大鼠随机分为假手术组(n=10)、缺血再灌注损伤组(IRI, n=45)和tempol预处理组(n=10)。IRI组采用右侧肾摘除左肾蒂夹闭50 min后松开制备缺血再灌注模型，分别于再灌注0、5、10、15、30、45 min及1、2 h处死动物取肾组织，Western印迹法观察p38活化情况。Tempol处理组动物同样制备缺血再灌注模型，术前1 h尾静脉注射tempol(100 mg/kg)，再灌注45 min取肾组织；假手术组行右侧肾摘除但不夹闭左肾蒂，术后45 min取肾组织。Western印迹法观察3组p38活化情况，分析肾组织丙二醛(MDA)含量，ELISA法检测肾组织肿瘤坏死因子α(TNF α)、白细胞介素1β(IL 1β)的含量。结果：大鼠肾组织磷酸化p38含量在再灌注早期(5 min)开始升高，45 min达到高峰，再灌注2 h仍较高(P<0.05)。与假手术组相比，IRI和tempol预处理组磷酸化p38含量明显升高(0.103±0.008 vs 2.025±0.136 vs 0.833±0.191，P<0.05)，且tempol预处理组低于IRI组(P<0.05)。3组间肾组织MDA、TNF α、IL 1β的含量检测结果与磷酸化p38结果类似(P<0.05)。结论：氧自由基介导的p38磷酸化在缺血再灌注引起的大鼠肾脏炎症性损害中具有重要作用；应用tempol可以抑制p38磷酸化，防治缺血再灌注损伤。

关键词：肾 再灌注损伤 p38丝裂原活化蛋白激酶类 氮氧化物 自由基清除剂 活性氧

Effect of tempol, a free radical scavenger, on p38 activation in rats with renal ischemia reperfusion injury Download Fulltext

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Abstract:

Objective: To investigate the activation of p38 signaling transduction cascade in renal ischemia reperfusion injury(IRI) and to study the effect of tempol, a free oxygen radical scavenger, on p38 activation. Methods: Male Sprague Dawley rats were randomly divided into sham operation group (n=10), IRI group (n=45) and IRI + tempol group(n=10). Animal IRI model was created by renal pedicle ligation (50 min) of the left kidney along with a contralateral nephrectomy followed by 2 h reperfusion. Rats were sacrificed on 0, 5, 10, 15, 30, 45 min, 1 and 2 h after renal reperfusion. Animals in IRI + tempol group were pretreated with tempol (100 mg/kg) 1 h before undergoing the same protocol as in IRI group; the kidney was harvested after 45 min of reperfusion. Animals in the sham operation group were subjected to contralateral nephrectomy without renal pedicle ligation and were sacrificed 45 min later. The renal p38 activities of the 3 groups were determined by Western blotting analysis. Malondialdehyde (MDA) content was detected and pro inflammatory cytokine TNF α, IL 1β levels were analyzed by ELISA. Results: Activation of p38 was observed in the kidney as early as 5 min after reperfusion and reached its peak 45 min after reperfusion and remained to be activated until 2 h after reperfusion(P<0.05). The activities of renal p38 in IRI and IRI + tempol group were markedly increased compared with that of the sham operation group(both P<0.05). Pretreatment with tempol significantly inhibited IRI induced p38 activation(P<0.05); it also decreased MDA activity and TNF α and IL 1β levels (both P<0.05). Conclusion: Our results demonstrate that reactive oxygen species mediated p38 activation plays an essential role in IRI induced renal inflammatory damage in rats, suggesting that inhibition of p38 activation by tempol may be used for prophylaxis and treatment of IRI.

Keywords: kidney reperfusion injury p38 mitogen activated protein kinases N oxides free radical scavengers reactive oxygen species

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