Nafamostat Mesylate Attenuates Ischemia-Reperfusion Induced Renal Injury via Inhibition of Apoptosis.

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OBJECTIVES

It has been reported that nafamostat mesylate (NM) inhibited inflammatory injury via inhibition of complementary activation in ischemic heart, liver and intestine. However, it has been little known that NM inhibits the apoptosis in ischemia-reperfusion (IR) injured kidney. We investigated whether NM attenuates IR renal injury and involves apoptosis inhibition.

METHODS

We used HK-2 cell and male C57BL/6 mice. C57BL/6 mice were divided into four groups; Sham, Nafamostat mesylate(NM,2mg/kg)+Sham, IR injury( IR injury; reperfusion 27 minutes after clamping of both renal artery and vein), and NM+IR injury. Kidneys were harvested 24hr after IR injury. BUN and serum creatinine(s-Cr) were measured 24 hrs after IR injury. We performed real time RT-PCR and immunohistochemistry for molecular study and H&E stain and Masson trichrome (MT) stain for histologic examination. For in vitro study, HK-2 cell were divided as into three groups; Control, IR-HK-2 (HK-2 cells were incubated for 6 hours with mineral paraffin oil for ischemic injury) and IR-HK-2+NM(2nM) groups. Cell survival and the magnitude of apoptosis were evaluated.

RESULTS

Figure 1. The levels of BUN and serum creatinine and renal tissue injury score in NM+IR injured mice were significantly lower than those of control IR mice (all, p<0.01).

Figure 2. Nafamostat mesylate treatment significantly improved cell survival in ischemic HK-2 cells (p<0.01). Renal Bax protein and mRNA expression were significantly increased in IR injured kidneys and ischemic HK-2 cells. NM treatment significantly decreased renal Bax expression (p<0.05).

Figure 3. Tissue injury score and TUNEL positive cells were significantly lower in NM+IR injured kidneys, comparing to control IR injured mice (p<0.05).

CONCLUSIONS

In conclusion, NM attenuates ischemia-reperfusion renal injury via inhibition of apoptosis.