Mol Cell Biochem
DOI 10.1007/s11010-013-1901-6

Involvement of the nuclear factor-κB pathway in the adhesion of neutrophils to renal tubular cells after injury induced by neonatal postasphyxial serum

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Received: 30 July 2013 / Accepted: 15 November 2013

Abstract Nuclear factor κB (NF-κB) plays an important role in the regulation of inflammatory proteins. However, it is unclear whether the NF-κB/intercellular adhesion molecule-1 (ICAM-1) pathway is involved in the adhesion of neutrophils and renal injury after hypoxia–ischemia (HI) in neonates. In this report we investigated whether NF-κB and its downstream molecule ICAM-1 were involved in renal injury induced by postasphyxial serum (PS) from neonates. Human renal proximal tubular (HK-2) cells were preincubated with 10 % fetal calf serum (control), 20 % neonatal PS, or 20 % PS plus pyrolidine dithiocarbamate (PDTC). The expression of IκBα, NF-κB p65, and ICAM-1 in HK-2 cells was determined by Western blot and/or immunohistochemistry. Nuclear translocation of NF-κB p65 in HK-2 cells was detected by immunofluorescence and Western blot. The ICAM-1 mRNA was determined by RT-PCR. Then HK-2 cells were cultured with neutrophils from neonates with asphyxia. After HK-2 cells had been cultured with neutrophils, we detected myeloperoxidase (MPO) activity, the leakage rate of lactate dehydrogenase (LDH), and cell viability. We found that PS preincubation resulted in significantly decreased IκBα expression and increased expression of NF-κB and ICAM-1, and facilitated the nuclear translocation of NF-κB in HK-2 cells. PS preincubation increased MPO activity, leading to elevated leakage rates of LDH and decreased cell viability after neutrophil exposure. Furthermore, the inhibition of NF-κB activity by PDTC significantly upregulated IκBα expression, decreased NF-κB and ICAM-1 expression, downregulated the nuclear translocation of NF-κB, and decreased MPO activity. This leads to decreased leakage rates of LDH and increased cell viability after neutrophil exposure. Our findings suggest that NF-κB/ICAM-1 pathway may be involved in neutrophil–endothelial interactions and neonatal renal injury after HI.

Keywords Postasphyxial serum · Nuclear factor-κB · Renal injury · Intracellular adhesion molecule-1 · Adhesion · Neonate

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Introduction

Asphyxia continues to be a major cause of death or later neurodevelopmental sequelae in neonates. After asphyxia, renal injury commonly occurs as a severe complication [1]. Renal cell death in hypoxia–ischemia (HI) is partly due to inflammation. Following HI, circulating neutrophils selectively infiltrate ischemic kidney tissues. Adherent neutrophils could release toxic products, which contribute to endothelial barrier injury and tissue destruction [2–4].

NF-κB, a ubiquitous transcription factor activated by various stimuli, is implicated in ischemia–reperfusion injury. NF-κB regulates the expression of genes associated with inflammation, which is likely to play a pivotal role in the pathophysiology of HI renal injury [5, 6]. Prevention of NF-κB could result in attenuated neutrophil infiltration [7].

Published online: 26 November 2013