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Protective effect of lyophilized recombinant human brain natriuretic peptide on renal ischemia/reperfusion injury in mice

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ABSTRACT. Brain natriuretic peptide (BNP) has a protective effect on acute injury of the heart, brain, and lung. However, its role in acute kidney injury (AKI) remains unclear. The aim of this study was to investigate the effect of lyophilized recombinant human BNP (lrh-BNP) on AKI and the underlying molecular mechanisms. An experimental model for AKI was established using an ischemia/reperfusion (I/R) procedure. Healthy adult BALB/c mice were randomized to the sham, I/R, and lrh-BNP-treated post-I/R (BNP + I/R) groups. Post-operatively, the BNP + I/R group was subcutaneously injected with lrh-BNP (0.03 $\mu g \cdot kg^{-1} \cdot min^{-1}$), whereas the other groups received saline at the same dose. Serum creatinine (Scr) and blood urea nitrogen levels were examined; tissue staining was performed to evaluate the degree of I/R injury (IRI). Ki67 positive staining of renal tubular epithelial cells was observed using immunofluorescence confocal laser scanning to assess the effect of BNP on cell proliferation after IRI. Inflammatory factor expression levels were detected to evaluate the effect of BNP on renal inflammation. Compared with the sham group, the I/R

group showed increased Scr levels, severe tubular injury of the renal outer medulla, increased Kim-1 mRNA expression, an increased number of infiltrative macrophages in the renal interstitium, and increased TNF-α, IL-1β, IL-6, MCP-1, and HIF-1α mRNA expression. BNP delivery significantly reduced all pathological changes in the I/R group. The protective role of BNP in murine renal IRI may be associated with its inhibition of renal interstitial inflammation and hypoxia and its promotion of renal tubule repair.

Key words: Renal ischemia/reperfusion injury; Inflammation; Hypoxia; Brain natriuretic peptide