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## **Hypercapnic Acidosis Attenuates Ischemia-Reperfusion Injury Associated Acute Kidney Injury in Rats**

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**Background:** Hypercapnic acidosis (HCA) preconditioning was suggested to attenuate ischemia-reperfusion (IR) injury of brain and lung, and underlying mechanism is uncertain. No study has assessed renoprotective effect of HCA preconditioning on renal IR injury. Here we investigate the effect and mechanism of HCA preconditioning on renal IR injury in rats.

**Methods:** Adult Sprague-Dawley rats are randomly exposed to humidified gas containing either FiCO<sub>2</sub> of 5% or room air only for 30 minutes before sham operation or clamping renal artery for 30 minutes. Three or 24 hours reperfusion followed. Urine, blood and kidney were obtained for biochemistry and histology. Protein level was determined by immunoblot.

**Results:** Histologically, less IR-related tubulointerstitial injury, leukocyte infiltration and tubular cell apoptosis were disclosed after HCA preconditioning. Functionally, HCA preconditioning preserved renal function after IR injury, reflected by better concentrating ability as well as low serum creatinine and urea nitrogen. Circulating TNF- $\alpha$ , interleukin (IL)-1 $\beta$  and IL-6 levels in response to IR is suppressed significantly in HCA group. HCA demonstrated anti-apoptotic effect by downregulating TRAF6-ASK1-p38/JNK pathway and reducing the cleavage of caspase 3 and PARP. HCA also suppressed NF- $\kappa$ B pathway to achieve anti-inflammatory effect and enhanced anti-stress ability by raising expression of heat shock protein 70 and heme oxygenase-1.

**Conclusions:** These results suggest that protective effect of HCA preconditioning on renal IR injury may be mediated by complex mechanisms including anti-apoptosis, anti-inflammation and anti-stress.