

## Preconditioning with AICAR Protects against Subsequent Renal Ischemia-Reperfusion Injury

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**Introduction :** Recently it was reported that acute renal ischemia rapidly activated AMP-activate protein kinase (AMPK). Preconditioning due to activation of AMPK might reduce I/R injury in the kidney, based on the key role of AMPK in preserving ATP. To evaluate this possibility, the effect of preconditioning with 5-aminoimidazole-4-carboxamide ribonucleoside (AICAR), AMPK activator before sustained ischemia was investigated

**Methods :** Adult male Sprague-Dawley rats weighing approximately 220-250 g were used. To induce renal ischemia, a laparotomy was performed and the blood supply to both kidneys was interrupted by the placement of a bulldog clamp at the level of the renal pedicles. Re-flow was initiated by removing the clamp. The following experimental groups were defined 1) Sham group, 2) I/R group: Animals were subjected to 45 minutes of bilateral renal ischemia and sacrificed 24 hours later. 3) AICAR+I/R group: administration of 100 mg/kg AICAR i.p 10 minutes before I/R, 4) araA+AICAR+I/R group: Same as group 3, but with previous administration of adenine-9-b-D-arabinofuranoside (araA), an inhibitor of AMPK, at 250 mg/kg i.p 10 minutes before AICAR.

**Results :** There was only faint AMPK phosphorylation in the sham group. After 10 minute of ischemia, and AICAR preconditioning however, Thr172a phosphorylation was increased ( $p < 0.01$ ). The serum BUN and creatinine levels were significantly decreased in AICAR preconditioning group ( $128.0 \pm 7.33$  mg/dL,  $4.18 \pm 0.27$  mg/dL vs.  $90.2 \pm 11.13$  mg/dL,  $2.58 \pm 0.7$  mg/dL,  $p < 0.05$ ), but these effects were abolished by araA+AICAR+I/R group. In quantitative analysis of tubular injury, tubular injury score in AICAR preconditioning group significantly decreased ( $p < 0.05$ ).

**Conclusion :** The AMPK activator AICAR has a protective effect against renal I/R injury.