

EDARAVONE PROTECTS AGAINST ISCHEMIA / REPERFUSION-INDUCED MORPHOLOGICAL AND FUNCTIONAL CHANGES IN RAT URINARY BLADDER

Hypothesis / aims of study

Edaravone, 3-methyl-1-phenyl-pyrazolin-5-one, is a newly developed radical scavenging agent that has been widely used for protection against ischemia / reperfusion (I/R) injury in patients with cerebral infarction. This compound has potent free radical scavenging and antioxidant actions without causing any serious side effects. And several reports showed that Edaravone protects against ischemia-reperfusion injury of the brain, heart, liver, and small intestine in rats. The present study investigated the effects of Edaravone on the I/R injury in the rat bladder.

Study design, materials and methods

Twenty four adult male Sprague-Dawley rats were divided in the four groups (N = 6): Groups 1 - 3 received 1 hour (hr) of ischemia followed by 1 hr reperfusion with saline and with Edaravone (1 and 3 mg/kg body weight), and group 4 were age-matched control rats. Animals were anesthetized with ketamine/xylazine solution. The bladder was exposed through a midline incision and both of the vesical arteries were identified. The *in vivo* ischemia was created by reversibly clamping the vesical arteries for 1 hr using a disposable vessel clip with a holding force of 60 grams. To remove the clips, reperfusion in the bladder was performed for 1 hr. Edaravone or saline were administered into femoral artery after reperfusion for 30 minutes. Following reperfusion, the bladders were removed and weighed, four longitudinal strips were obtained. One of the bladders strips, smooth muscle cell phenotypic expression in the electron micrographs were investigated. The number of contractile phenotype and non-contractile (synthetic) phenotype which were recognized according to the morphological criteria was counted and the ratio of non-contractile to contractile (nc/c) phenotype was calculated. Other bladders strips were mounted in an isolated muscle bath for physiological studies; the responses to electrical field stimulation (FS) at 2, 8 and 32 Hz., carbachol (20 μ M) and KCl (120 mM). The maximal contractile response were recorded digitally and analyzed.

Results

The ratio of nc/c phenotype in the control group was approximately 0.16. In the I/R with saline group, the ratio of nc/c phenotype became approximately 0.78, whereas in Edaravone treatment groups became approximately 0.40. The contractile response of bladder strips to FS, carbachol and KCl were determined. The maximal contractile responses to FS (2, 8 and 32 Hz.) were reduced by approximately 50%, carbachol responses were reduced by 33%, and KCl responses were reduced by 45% following I/R with saline compared to the control group. Edaravone administration resulted in the protection of the morphologic change and contractile responses to both FS and carbachol whereas the responses to KCl were not affected by the agent.

Interpretation of results

We have demonstrated in present study that I/R lead to bladder dysfunction as well as to the induction of lipid peroxidation. Both bladder dysfunction and the induction of lipid peroxidation are prevented by Edaravone. This theory suggests that antioxidants, Edaravone (free radical scavengers) and other neuroprotective medications may have therapeutic benefit in patients with bladder outlet obstruction.

Concluding message

Our findings demonstrate that Edaravone has potentiality protective effect on I/R induced damage in rat bladder.

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ANIMAL SUBJECTS: This study followed the guidelines for care and use of laboratory animals and was approved by Kinki University School of Medicine