

PROTECTIVE EFFECT OF ALLOPURINOL AGAINST ISCHEMIA/REPERFUSION INJURY IN RAT URINARY BLADDERS

Hypothesis / aims of study

Bladder ischemia-reperfusion (I/R) injury results in the generation of reactive oxygen species (ROS) and markedly elevates the risk of lower urinary tract symptoms (LUTS). Allopurinol is an inhibitor of xanthine oxidase (XO) and thus can serve as an antioxidant that reduces oxidative stress.

Study design, materials and methods

The 45 animals in the study were divided into three groups: the saline-pretreated sham-operated group (Sham + S), the saline-pretreated ischemia-reperfusion group (I/R + S), and the allopurinol-pretreated group (I/R + Allo). The bladder tissue of these rat groups was isolated to assess the contractile responses, XO activity, TNF- α , MDA levels, histologic analysis (Dihydroethidium Stainings). Expression of MAPKs and apoptotic pathway (such as Erk, Jnk, P38, Bax, Bcl-2 and phospho-Erk, -JNK, p38) have detected by Western blotting.

Results

I/R injury reduced the in vitro contractile responses of longitudinal bladder strips, elevated XO activity in the plasma and bladder tissue, increased the bladder levels of tumor necrosis factor- α (TNF- α), c-Jun N-terminal kinase (JNK), and p38 mitogen-activated protein kinase, reduced the bladder levels of extracellular regulated kinase (ERK), and decreased and increased the bladder levels of Bcl-2 and Bax, respectively, thereby decreasing the Bcl-2/Bax ratio. Allopurinol markedly enhanced the expression of Phospho-ERK and weakened the expression of Phospho-JNK and p38 compared to I/R injury group. I/R injury also elevated lipid peroxidation in the bladder. Allopurinol treatment of the rats for 2 weeks before and 1 week after the I/R injury was generated significantly ameliorating all I/R-induced changes. Moreover, an in situ fluorohistological approach also showed that allopurinol reduces the generation of intracellular superoxides enlarged by I/R injury.

Interpretation of results

The beneficial effects of allopurinol reducing ROS production may be mediated by normalizing the activity of the ERK, JNK, and Bax/Bcl-2 pathways and by controlling TNF- α expression.

Concluding message

The present study showed that XO mediated ROS formation may play an important role in the pathogenesis of bladder I/R injury and that allopurinol protects against apoptotic state.

References

1. Eur J Pharmacol. 2015 May 5;754:92-7
2. Neurourol Urodyn. 2014 Jan;33(1):54-8

Disclosures

Funding: no **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** All animal experiments followed a protocol that was approved by the ethics committee on animal research at Chungnam National University, Daejeon, Korea.