

## **PROTECTIVE EFFECTS OF LEUKOTRIENE RECEPTOR ANTAGONIST-MONTELUKAST AGAINST PROTAMINE SULFATE INDUCED BLADDER INJURY**

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**INTRODUCTION & OBJECTIVES:** This morphological study aims to evaluate the effects of a cys-leukotriene-1 receptor antagonist, montelukast, on protamine sulfate (PS) induced bladder injury. Leukotrienes (LTs) are synthesized by the bladder and exert their actions by binding to and activating various receptors. They have been shown experimentally to play a role in inflammatory mechanisms. In human detrusor myocytes, the presence of specific leukotriene D4 receptors are shown and potential pathophysiological role of leukotriene D4 in patients with interstitial cystitis and other bladder disorders are implicated.

**MATERIAL & METHODS:** Wistar albino female rats were catheterized and intravesically infused with phosphate buffered solution (control group) or protamine sulfate (bladder injury group) dissolved in phosphate buffered solution, twice (12 hours interval) only. In the protamine sulfate + montelukast group (bladder injury + montelukast group) after the protamine sulfate instillation, montelukast was injected 10mg/kg intraperitoneally for three days. The morphology of the urinary bladder was investigated with light and electron microscopy. The number of mast cells in the mucosa, mucosal alterations, intercellular junctions, surface topography and glycosaminoglycan (GAG) layer were evaluated. Lipid peroxidation was also performed.

**RESULTS:** In the bladder injury group, ulcerated areas, irregularity of urothelium, increased number of mast cells, vacuole formation, dilated perinuclear cistern, formation of pleomorphic and uniform microvilli and dilatations in the intercellular areas in the urothelium were observed. In the bladder injury + montelukast group a relatively normal urothelial topography, GAG layer and decreased number of mast cells in the mucosa, some dilatations between the intercellular areas, less uniform microvilli, regular perinuclear cistern and tight junctions were observed. Increased MDA levels as a result of protamine sulfate induction had led us to propose that free radicals may play a crucial role in this injury.

**CONCLUSIONS:** The significant decrease in MDA levels in protamine sulfate+montelukast group was in accordance with the histologic findings so in conclusion montelukast appears to exert an urothelial protective activity in bladder injury model.