Alterations in Peripheral Purinergic and Muscarinic Signaling of Rat Bladder After Long-Term Fructose-Induced Metabolic Syndrome

Introduction and Objective: We explored the pathophysiologic mechanisms of long-term fructose-induced lower urinary tract symptoms (LUTS) in rats.
Material and Methods: Male Wistar rats were fed with fructose for 3 or 6 months. Biochemical and transcytometric parameters were compared between fructose-fed and age-matched normal-diet rats. Pelvic nerve and external urethral sphincter-electromyogram activity recordings were performed to investigate fructose effects on neural control of bladders. Mitochondrial structure, ATP and acetylcholine content and purinergic and muscarinic cholinergic receptors were examined. Cytosolic cytochrome C staining by western blot and immunocytochemistry for mitochondrial injury and PGP 9.5 stain for nerve density were also determined.
Results: The fructose-fed rats with higher plasma triglyceride, LDL, and fasting glucose levels displayed LUTS with increased frequency and suppressed voiding contractile amplitude in phase 1 and phase 2 duration vs. normal diet control. Fructose feeding altered the firing types in pelvic afferent, efferent nerve and external urethral sphincter-electromyogram activity. Increased mast cell number, disrupted and swollen mitochondria, increased cytosolic cytochrome C stain and expression and decreased nerve density in bladder smooth muscle layers appeared in the fructose-fed rats. Fructose feeding also significantly reduced ATP and acetylcholine content and enhanced protein expression of postsynaptic P2X1, P2X2 and P2X3 purinergic receptors and M2 and M3 muscarinic cholinergic receptors expression in the smooth muscles of urinary bladder.
Conclusion: Long-term fructose feeding induced neuropathy and myopathy in the urinary bladders. Impaired mitochondrial integrity, reduced nerve density, ATP and acetylcholine content and upregulation of purinergic and muscarinic cholinergic receptors expression may contribute to fructose-fed induced bladder dysfunction.