440

Munoz A[1], Romain Z[1], Munch E[1], Boone T[2], Smith C[1], Somogyi G[1]
1. *Baylor College of Medicine,* ***2.*** *The Methodist Hospital*

EARLY DIABETES IMPAIRS NON-ADRENERGIC NON-CHOLINERGIC CONTRACTIONS IN THE URINARY BLADDER OF FEMALE RATS

Hypothesis / aims of study

Electrical stimulation of the rat bladder induces acetylcholine and ATP release to elicit bladder contractions. Muscarinic antagonists are not fully effective in inhibiting neurally evoked bladder contractions due to a non-adrenergic, non-cholinergic (NANC) contractile component. The NANC response can be altered during pathology. In this project, we investigated the NANC response in rat bladder strips from diabetic rats in the presence of the cholinergic agonist carbachol (CCh). We also measured changes in the purinergic response to the P2X agonist alpha,beta-methylene ATP (ab-me ATP) following muscarinic receptor activation. Finally, we determined the change in NANC response to carbachol induced pretreatment of the preparation with a muscarinic antagonist.

Study design, materials and methods

All animal experiments were carried out in accordance with the National Institute of Health Guidelines for the Care and Use of Laboratory Animals, and were approved by the Institutional Animal Care and Use Committee. Female Sprague-Dawley rats received a single injection of streptozotocin (65 mg/kg). Experiments were carried out at 4 weeks after induction of diabetes. Bladder strips were electrically stimulated (ES) with square wave impulses (0.25 ms, 20 Hz, 200 shocks) at 100 Volts every 100 s. In our protocols, strips were contracted with 50uM ab-me ATP, then washed and ES started. In protocol-A, strips received 50µM CCh followed by inhibition of the muscarinic component with 1 µM atropine while maintaining electrical stimulation throughout. At this point, ES was stopped and a second application of ab-me ATP was carried out. In protocol B the application order of carbachol and atropine was inverted, otherwise conditions were the identical.

Results

Initial activation of purinergic receptors produced an equal contractile response in both groups; however, contractions following cholinergic activation and blockage of the muscarinic component (protocol A) caused a reduction of the second ab-me ATP application of 50% in both groups. Following protocol-B, we found that control strips retained their NANC response, but the diabetic strips group continued to have an impairment of 60%.

Interpretation of results

Early diabetes affects purinergic signaling in the urinary bladder of female rats. Inhibition of muscarinic receptors does not ameliorates the NANC response observed in diabetic bladders

Concluding message

This study provides important insight into the purinergic and nitrergic signaling pathways in urinary bladder hyperactivity during diabetes. Understanding these pathways might lead to novel therapies.

Specify source of funding or grant	**Supported by NIH (RO1-DK069988) and the Smith Neurourology Fund.**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Baylor College of Medicine/Institutional Animal Care and Use Committee**