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TIME-COURSE OF CHANGES IN THE DIABETIC BLADDER DYSFUNCTION

Hypothesis / aims of study

Clinical and laboratory investigations report both overactive and atonic diabetic bladder dysfunction (DBD). We explored whether DBD in a rat diabetes mellitus (DM) model varies with DM duration.

Study design, materials and methods

Thirty male Sprague-Dawley rats with DM induced by single intraperitoneal injection of STZ 60 mg/kg were serially sacrificed at 3,6,9,12 and 20 weeks as were 4 to 6 age-matched controls per group. After urethane anesthesia (1.2 g/kg, s.c.), cystometrograms were conducted via suprapubic catheter. Bladders were removed and two 4×10 mm muscle strips suspended in a 20 ml organ bath. Strips were stretched to a passive tension with 2 g, left 30 minutes to equilibrate and then stimulated, with appropriate washouts, by varying levels of KCl (30 mM-120 mM), electrical fields (EFS, 0.5-32 Hz, 10 sec with 0.5 msec duration at supramaximum voltage every 2 min), adenosine 5'- triphosphate (ATP, 100 µM-30 mM), and carbachol (CCh, 10 nM-100 µM). Isometric contractions were recorded by data acquisition software. Statistical significance was assessed in fixed or mixed effects linear statistical models, after Box-Cox transformation as needed.

Results

Relative to controls, micturition peak pressure was reduced and resting pressures immediately and 45 minutes post-voiding were elevated in 12 and 20 week old DM rats; these differences were absent or reversed at 3 and 6 weeks ($p<.0001$ for each interaction). Responsiveness to ATP and CCh was generally higher in DM than control rats, and responses to CCh, KCl, and EFS in DM decreased substantially between 9 and 12 weeks. These decreases were sustained at week 20 and not seen in control rats ($p=.16, .04, .03$ for the respective interactions). Basal bladder pressure, threshold pressure for leak, and bladder capacity increased with age ($p=.014, <.0001, <.0001$) and were elevated in DM rats (each $p<0.001$). Bladder compliance was proportionally elevated and micturition interval proportionally reduced in DM relative to controls (both $p<.0001$).

Interpretation of results

Changes in the cystometrogram and contractility of the detrusor vary in correlation to duration of diabetes with increased voiding pressure before 9 weeks and decreased voiding pressure after 9 weeks.

Concluding message

Bladder dysfunction in STZ-induced DM rats may be related to a change in contractility from early (<12 weeks post-induction) to later (≥12 weeks) disease.

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