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CELLULAR REMODELLING IN THE RAT DIABETIC BLADDER: CORRELATION WITH ENHANCED CONTRACTILITY

Hypothesis / aims of study

Diabetes is an increasingly prevalent condition worldwide and is associated with a range of comorbidities including bladder dysfunction (1). The diabetic bladder exhibits an overactive phenotype arising from neurogenic and myogenic mechanisms; moreover, changes in the cellular architecture of the bladder wall occur. The purpose of the present study was to investigate cellular remodelling in the rat diabetic bladder and correlate with in vitro contractility.

Study design, materials and methods

Bladders were removed from Sprague-Dawley female rats – either non-injected controls or diabetics following a single injection of streptozotocin. Tissue strips were prepared as full thickness or detrusor layers (mucosal layer removed) and studied with in vitro myography. Tissues were also processed for immunohistochemistry. Data are presented as mean±SEM and analysed by ANOVA/Student's t-test.

Results

Diabetic rats (N=8) had significantly lower body mass than non-injected controls (N=6; $p<0.042$) however; mean bladder/body mass ratio for diabetics (1.96±0.42, N=8) was significantly greater than controls (0.48±0.05, N=6; P=0.01) indicative of smooth muscle hypertrophy. This was confirmed by imaging protocols. Extensive networks of Interstitial Cells (IC), labelled with PDGFRα were distributed in the lamina propria and detrusor layer of control bladders. In diabetic bladders, PDGFRα^{+}-IC were notably disrupted in the detrusor layer but were present in the in the lamina propria.

Spontaneous activity in full thickness and detrusor strips from diabetic bladder was significantly greater than controls. Control contraction amplitude in full thickness strips was 0.12±0.03g, n=8, N=4) compared with diabetic strips 0.22±0.03g (n=12, N=6, p=0.017).

Neurogenic contractions, evoked by electrical field stimulation in the same preparations, were of greater amplitude in diabetic strips across a range of frequencies in both full thickness and detrusor preparations. Contraction amplitude at 16Hz in full thickness control strips was 3.94±0.52g (n=8, N=4), smaller than in diabetic strips 5.96±0.43g (n=12, N=6, P<0.01).

Carbachol-evoked contractions (1μM) were significantly greater in diabetic strips whether or not the mucosal layer was present. In full thickness control strips, carbachol-evoked amplitude was 1.49±0.29g (n=10, N=5, $p<0.05$) compared with 3.01±0.42g (n=12; N=6; $p<0.05$).

Interpretation of results

Enhanced contractility in the diabetic bladder including spontaneous activity, neurogenic and agonist-evoked contractions occurs in the presence or absence of the mucosal layer. This altered contractility is correlated with smooth muscle hypertrophy and disruption of detrusor IC.

Concluding message

Cellular remodelling in the STZ-diabetic bladder is associated with augmented spontaneous, neurogenic and agonist-evoked contractions. The underlying mechanisms are complex and remain to be elucidated but are shown in the present study to involve multiple cellular components within the bladder wall.

References

1. Kirschner-Hermanns R, et al, 2011. Neurourol Urodyn. 2012 Mar;31(3):359-64.

Disclosures

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