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INCREASED BASAL AND STIMULATED SPONTANEOUS ACTIVITY IN DIABETIC OVERACTIVE BLADDER

Hypothesis / aims of study

The myogenic basis of bladder overactivity has recently become a focus of interest and may involve increased detrusor muscle spontaneous activity (1). The pathophysiological mechanisms underlying this remain unclear. This study aims to assess basal spontaneous phasic activity (SA) and stimulated SA in diabetic overactive bladder.

Study design, materials and methods

Strips of detrusor muscle were isolated from male Wistar rats (200-250g) 1, 4, 8 and 12 weeks following streptozotocin (65mg/kg, i.p.) administration or weight matched controls and were mounted under 2g tension in Krebs-bicarbonate solution at 37°C in tissue baths. Isometric tension was measured, via UF1 force transducers connected to a Powerlab using Chart software. Spontaneous rhythmic activity was recorded and expressed as mean area under the curve (AUC±SEM). Following equilibration (60 minutes), the effect of muscarinic modulation with low concentrations of carbachol (CCH) (0.05-0.5uM) on SA was assessed and expressed as increase beyond basal SA.

Results

Basal SA was seen in around 30% of control and over 50% of the 1, 4 and 8-week diabetic rat bladder detrusor strips but not in strips from 12 week diabetic rats. This basal SA was increased in strips from 1 (AUC= 98.321±12.53, $p<0.05$), 4 (AUC=119.29±17.86, $p<0.05$) and 8 weeks (AUC=112.23± 24, $p<0.05$) diabetic rats compared to controls (AUC=59.56±5.52). Low concentrations of CCH increased basal SA in a concentration dependent manner in all groups (table 1) and these responses were enhanced in diabetic groups (table 1).

	0.05uM CCH(AUC)	0.1uM CCH(AUC)	0.5uM CCH(AUC)
controls(n=8)	4.86±5.02	21.744±5.16	51.24±10.60
1 week (n=12)	7.95±3.69	58.67±10.37*	290±29.91***
4 week (n=4)	10.40±2.45	46.25±14.74	213.85±54.24**
8 week (n=8)	19.13±5.31	87.37±18.77**	218.17±32.20***
12 week (n=8)	7.65±2.53	38.54±6.94	163.58±25.04**

Table 1. Data is presented as increase in SA (AUC±SEM) induced by CCH beyond basal levels. *$p<0.05$,**$p<0.01$,***$p<0.001$

Interpretation of results

Detrusor muscle strips from STZ diabetic rat bladders show increased basal spontaneous activity up to 8 weeks following induction of diabetes. This spontaneous activity can be modulated by muscarinic stimulation and diabetic bladders appeared to be more sensitive to this modulation compared to controls. 12-week diabetic detrusor strips do not show any basal SA. However, SA can be induced by muscarinic modulation in these tissues, but there is a lower sensitivity compared to other diabetic groups.

Concluding message

Detrusor muscle strips from STZ diabetic rat bladders show increased basal spontaneous activity up to 8 weeks following induction of diabetes with no basal spontaneous activity at 12-weeks. This spontaneous activity can be modulated by muscarinic stimulation and diabetic bladders are more sensitive to this.

References

1) *Urol* (1997) 50 (suppl 6A):57-67

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