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NONTRAUMATIC URETHRAL DYSSYNERGIA IN THE NEONATALLY ESTROGENIZED MALE RAT

Aims of the study

Males chronically treated with estrogen develop bladder outlet obstruction with complete urinary retention, hypertrophy of the bladder wall as well as squamous metaplasia of the urethral epithelium. Enlarged bladder and thickened bladder wall occasionally with bladder stones have also been seen in adult male mice treated neonatally with estrogen, associated with lower voided volumes, higher voiding frequencies and decreased ratio of the urinary flow rate to the bladder pressure, which are consistent with the infravesical obstruction (1). Because of the lack of electromyographic recordings, these studies did not allow more specific understanding of the failure mechanism. The larger body size of the rat allowed accurate recordings of the electrical activity of proximal rhabdosphincter with transvesical cystometry (2) and the flow from the distal urethra (3). We recently observed that the shape of the electrical activity shows in single EMG activities of the proximal rhabdosphincter a depolarisation with overcoming transient repolarisation ending to another depolarisation in association with co-occurring flow peaks. In the present study, we have recorded the electrical activity of the proximal rhabdosphincter in the neonatally estrogenized rat known to have an infravesical obstruction with an unknown failure mechanism.

Methods

Adult neonatally estrogenized rats (neoDES) (diethylstilbestrol, DES treatment) were used in the study. The rats were anaesthetized. The bladder, anterior surface of the proximal rhabdosphincter and distal urethra were exposed. A 20G i.v. infusion cannula was inserted through the bladder apex into the lumen, for saline (0.9% NaCl) infusion into the bladder and its pressure measurements (2). Micturition was evoked physiologically by the infusion of the saline. An ultrasonic flow probe was used for measurement of the urine flow rate from the distal urethra. At the same time with the measurements of transvesical cystometry and flow rate, the electrical activity of the proximal rhabdosphincter was measured extracellularily with a suction electrode (4). Three representative micturitions were taken from each rat for further analysis.

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Results

The depolarisation amplitude of the proximal rhabdosphincter EMG was increased significantly ($p = 0.02$) in neoDES rats (3.0 mV, SD 0.78) compared to the controls (Co) (2.6 mV, SD 0.87). The transient repolarisations were absent or highly reduced in neoDES {-0.22 mV (SD 0.55)} compared to Co rats {+0.27 mV (SD 0.83), $p = 0.04$}. In the neoDES rats, the pressure oscillations showed higher maximal bladder pressure than Co rats, {neoDES 42.1 mmHg (SD 6.4) and Co 37.7 mmHg (SD 4.9), $p = 0.01$}. NeoDES rats showed decreased mean flow rates {neoDES, 2.3 ml/min (SD 1.01) and Co 4.1 ml/min (SD 0.1), $p < 0.0001$}. The micturition of the neoDES rats consisted usually of several voidings.

Conclusions

The alterations in the structure and electrical activities of the urethral musculature suggest that neonatal exposure to diethylstilbestrol (DES) predispose the male rat to urethral dyssynergia, seen as altered EMG activity of the proximal rhabdosphincter with lacking or reduced transient repolarisation. By definition, urethral dyssynergia means inappropriate contraction or failure of complete relaxation of the urethral musculature during detrusor contraction. The reduced flow rate and elevated bladder pressure in neoDES indicate infravesical obstruction. Voiding was still possible in neoDES animals regardless of the altered electrophysiology.

References

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