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A NEW MODEL OF INTRINSIC SPHINCTERIC DEFICIENCY IN THE RAT: ELECTROCAUTERIZATION

Aims of Study

Intrinsic sphincteric deficiency (ISD) denotes a malfunction of the distal urethral sphincter. In most patients with ISD, significant myogenic damage is present in the sphincter (1). Such damage can result from direct injury to the sphincter muscle, injury to the pudendal nerve with subsequent denervation of the sphincter, or both. Other investigators have described rat models for ISD. Lin and associates simulated birth injury by using a modified 12 French Foley catheter to distend the vagina for 4 hours (2). This investigator showed that vaginal distention produced extensive disruption and thinning of the striated muscle layer within the urethral wall. Another rat model for ISD involved transecting the pudendal nerves bilaterally (3). However, this injury was reversible after 3 months. Our objective was to produce a rat model of ISD that would approximate the injury seen most often clinically, a combination of both myogenic and nerve damage to the sphincter.

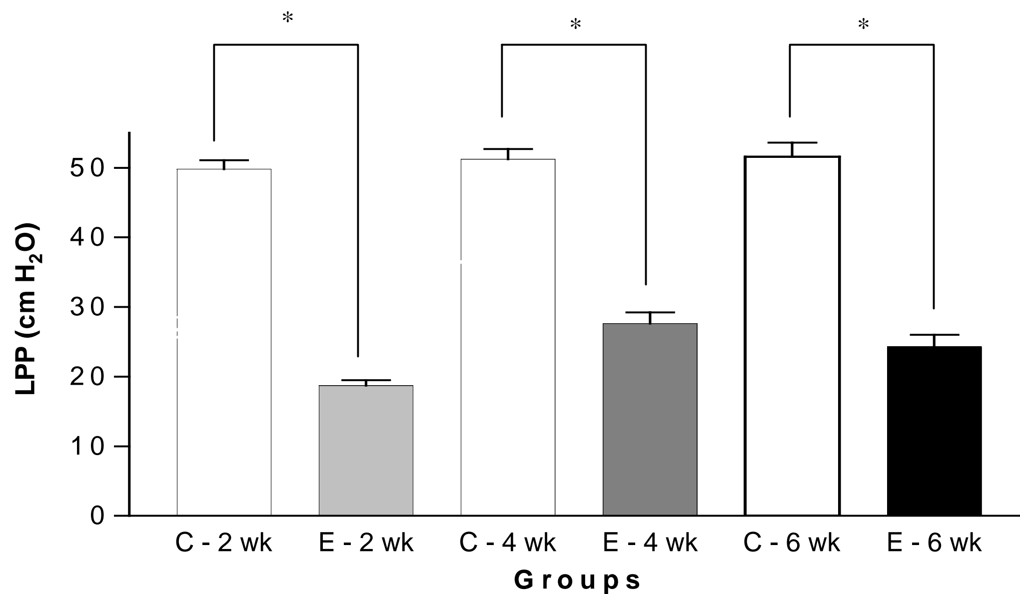
Methods

Under halothane anesthesia (2%), 18 adult female Sprague-Dawley rats underwent cauterization of tissues lateral to both sides of the mid-urethra to produce ISD. The cauterization began 1 cm below the bladder neck and extended caudally on each side to the mid-urethra, at the superior edge of the symphysis pubis. A fine tip, high temperature cautery was used to perform the cauterization. Each side was cauterized for 30 seconds. The rats were divided into 3 groups of 6 rats each and followed for 2, 4, and 6 weeks. Under urethane anesthesia, the rats underwent cystometry to evaluate the effects of the cauterization on bladder function. Sphincteric function was then studied by using a vertical tilt table/intravesical pressure clamp model to measure leak point pressures (LPPs). Intravesical pressure was increased in 1-3 cm H_2O steps from zero upward until fluid was seen leaking from the urethral meatus. The pressure at which leakage occurred was defined as the LPP. The average of three consecutive LPPs was taken as a data point for each animal. Subsequently, intravenous α-bungarotoxin (333 μg/kg) was administered to suppress further sphincteric activity. Approximately 10 minutes after the injection of α-bungarotoxin, 3 more LPPs were obtained. Resultant muscle damage and nerve atrophy within the mid-urethra were assessed histologically with fast myosin heavy chain and anti-protein gene product (PGP) 9.5 staining, respectively. As a control, 9 rats, divided into 3 groups of 3 rats each, underwent a sham operation during which the urethra was exposed but not cauterized. Subsequent LPP testing was performed in these rats at 2, 4, or 6 weeks.

Results

Cystometry in all cauterized rats showed bladder contractions that were comparable in amplitude and duration to those of the control rats. Between cauterized and control rats, no difference was noted in either the intercontraction interval or the maximal detrusor pressure during voiding. As shown in the figure, the mean LPPs of the rats 2, 4, and 6 weeks after cauterization were 18.7$\pm$0.8 cm H_2O, 27.6$\pm$1.6 cm H_2O, and 24.3$\pm$1.7 cm H_2O, respectively. The mean LPPs of the rats 2, 4, and 6 weeks after the sham operation were 49.8$\pm$1.3 cm H_2O, 51.2$\pm$1.5 cm H_2O, and 51.6$\pm$2.0 cm H_2O, respectively. When compared to time matched control groups, the decreased LPPs in each cauterized group were significantly lower ($p<0.001$). The administration of α-bungarotoxin further reduced the LPP in the cauterized rats. However, the reduction was only 40% of that seen in the control rats. Histological analysis showed disruption of the striated muscle layer and fewer nerves in all cauterized groups.

Figure: The effect of electrocauterization on LPP. When compared to respective time matched control groups the decreased LPPs seen in each cauterized group were significantly lower (∗ denotes $p<0.001$ for each of the 3 pairs of groups). C denotes control, and E denotes electrocauterization.



Conclusions

This electrocauterization model produced no change in bladder function and low LPPs that, after 2 weeks, were maintained for up to 6 weeks. Because the reduction in LPP for the cauterized rats was only 40% of that seen in the control rats, electrocauterization significantly reduced the neurally mediated sphincteric response. Histology suggested that damage to striated muscle and nerves contributed to the change in LPP in this model for ISD.

References

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