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Title: INFLUENCES OF BILATERAL HYPOGASTRIC NERVE TRANSECTION ON VOIDING DYSFUNCTION IN THE RAT WITH SPINAL CORD INJURY

Aims of Study

Spinal cord injury (SCI) rostral to the lumbosacral level causes lower urinary tract dysfunction characterized by detrusor hyperreflexia, incontinence and un-coordinated bladder and external urethral sphincter (EUS) activity, termed detrusor-sphincter dyssynergia (DSD) [1]. DSD increases outlet resistance and induces high intravesical pressures during voiding that can damage the upper urinary tract. Thus, drug therapies or surgical procedures that diminish urethral resistance and/or intravesical pressure would be helpful in reducing urinary tract complications associated with DSD. Numerous studies have revealed that sympathetic efferent signals passing through the hypogastric nerve (HGN) and the lumbosacral sympathetic chain control the bladder neck (BN) and proximal urethra (PU) that form the internal urethral sphincter [2]. Excitatory sympathetic input to the BN/PU maintains closure of the outlet for urine during storage period. Therefore, it is presumed that reduction of urethral resistance to improve voiding can be induced by diminishing sympathetic transmission to the BN/PU by drug or surgical treatment. The present studies were conducted to determine whether bilateral section of HGNs, which provided the major sympathetic outflow to BN/PU [3], could improve voiding function by reducing urethral resistance in conscious female SCI rats.

Methods

Conscious, female Sprague-Dawley rats (250-300 g) with spinal cords chronically transected (2-3 week-postspinalized) at Th7-9 (n=24) were used in these studies. Rats were placed in a restraining cage (Ballman cage) and bladder activity was monitored *via* the cystometric catheter connected to a pressure transducer. Cystometric recordings were performed by continuously infusing physiological saline (0.21 ml/min) at room temperature into the bladder to elicit repetitive voidings. Voiding properties during cystometry were evaluated in acutely, bilaterally HGNs-sectioned (n=12) and HGNs-intact (n=12) conditions in SCI rats. Parameters measured included: voided volume (VV), residual volume (RV), volume threshold for inducing micturition (VT), voiding efficiency (VE), pressure threshold for inducing micturition (PT), micturition pressure (MP), bladder compliance (CP) and bladder contraction duration (BCD).

Results

RV, VT, MP and CP in SCI rats with sectioned HGNs were 29 %, 65 %, 67 % and 69 %, respectively, of those in SCI rats with intact HGNs (Table 1), whereas VV, PT and BCD in the two groups were similar (data not shown). VE in HGNs-sectioned group was 36 % higher than that in HGNs-intact group.

TABLE 1

	RV (ml)	VT (ml)	VE (%)	MP (cm H_2O)	CP (ml/cm H_2O)

HGNs - *Intact* (n=12)	0.63 ∀ 0.18 (0.11-2.34)	1.33 ∀ 0.21 (0.68-3.10)	58 ∀ 7 (24-86)	49.3 ∀ 4.3 (24.9-82.9)	0.16 ∀ 0.02 (0.08-0.33)
HGNs - *Sectioned* (n=12)	0.18 ∀ 0.02* (0.12-0.31)	0.87 ∀ 0.08* (0.56-1.44)	79 ∀ 2** (70-86)	33.2 ∀ 1.7** (21.5-42.7)	0.11 ∀ 0.01* (0.08-0.19)

All values are expressed as mean ∀ S.E.M. Numbers in the parentheses are measured ranges. The values in "HGNs-sectioned" group are different from the ones in "HGNs-intact": *p<0.05, **p<0.01 (unpaired *t* test).

Conclusions

In conscious female SCI rats, relaxation of the BN/PU by bilateral section of HGNs decreased MP, reduced RV and improved VE. Although a surgical procedure was used to eliminate sympathetic innervation in the present studies, the results set the stage for utilization of a rat model in order to compare the efficacies of various treatments directed toward reducing urethral outlet resistance. Local injections of botulinum toxin into EUS have been clinically used to reduce DSD in human SCI patients [4]. In addition, our previous studies raised the possibility that injection of ∀-bungarotoxin might also be useful to treat DSD in rats [5]. The present results indicate that ∀-adrenoceptor antagonists that would block sympathetic input to the BN/PU or section of HGNs could be useful in human SCI patients for reducing urethral outlet resistance.

Source of funding

This study was supported by National Institutes of Health grants DK-49430 (W.D.) and DK-51402 (W. D.).

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