Electrical Stimulation of the Urethra Evokes Bladder Contractions in a Woman With Spinal Cord Injury

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Abstract

Objective: Electrical stimulation of pudendal urethral afferents generates coordinated micturition in animals and bladder contractions in men after spinal cord injury (SCI), but there is no evidence of an analogous excitatory urethra-spinal-bladder reflex in women. The objective of this study was to determine whether electrical stimulation of the urethra could evoke bladder contractions in a woman with SCI.

Case Report: A 38-year-old woman with a C6 ASIA A SCI who managed her bladder with clean intermittent catheterization and oxybutynin demonstrated neurogenic detrusor overactivity on urodynamics. Oxybutynin was discontinued 2 days prior to urodynamic testing with a custom 12F balloon catheter mounted with ring-shaped electrodes located in the bladder neck, mid urethra, and distal urethra. The inflated balloon was placed against the bladder neck to stabilize the catheter electrodes in place along the urethra. However, the balloon limited emptying during contractions. Urodynamics were performed at a filling rate of 25 mL/minute until a distention-evoked bladder contraction was observed. The urethra was stimulated over a range of bladder volumes and stimulus parameters to determine whether electrical stimulation could evoke a bladder contraction.

Findings: Electrical stimulation via urethral electrodes evoked bladder contractions that were dependent on bladder volume (>70% capacity) and the intensity of stimulation.

Conclusions: This is the first report of an excitatory urethra-spinal-bladder reflex in a woman with SCI. Future studies will determine whether this reflex can produce bladder emptying.

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Potential Conflicts of Interest: (1) Four of the authors (MEB, JHG, WMG, and JWB) are named inventors on patents related to the discovery described in the manuscript, and two of these (WMG and JWB) have a royalty agreement; (2) three of the authors (MEB, JHG, and JWB) are salaried employees of NDI Medical LLC; (3) WMG is a paid consultant of NDI Medical LLC and Medtronic Inc; (4) MJK received grant sponsorship from

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INTRODUCTION

Spinal cord injury (SCI) leads to voiding dysfunction, including neurogenic detrusor overactivity, detrusor sphincter dyssynergia, and poor voiding efficiency. The inability to empty the bladder voluntarily can result in medical complications, including urinary tract infections and damage, social frustration, and a decrease in quality of life (1,2). There is a large unmet need for a simple system to empty the bladder in persons with limited dexterity.

The traditional view of coordinated reflex micturition holds that brain stem control is required to coordinate bladder and sphincter activity, and the ability to produce coordinated micturition is lost following SCI (3,4). However, recent studies in animals with SCI challenge

this view; electrical stimulation of pudendal urethral afferents evoked micturition-like activity (bladder contractions coordinated with a decrease in external urethral sphincter activity) and bladder emptying (5–10).

It may be possible to translate this approach from animals (6,8) to restore bladder emptying in humans if an analogous spinal micturition reflex can be demonstrated in humans after SCI. The first step of demonstrating an excitatory urethra-spinal-bladder reflex has been reported in men but not in women. Intraurethral stimulation evoked bladder contraction in 4 of 5 men with complete SCI (11), and direct stimulation of the compound pudendal nerve evoked increases in bladder detrusor pressure in 2 men with SCI (12). However, it remains unclear whether the same bladder responses can be evoked in women with SCI.

SCI can have a profoundly negative impact on women, who do not have the option of a condom catheter and may lack the physical dexterity for self-catheterization. The objective of this case study was to determine whether intraurethral electrical stimulation could evoke bladder contractions in a woman with SCI. This is the first published account of bladder contractions evoked by electrical stimulation of the urethra in a woman with SCI. The goal is to develop a medical device that uses electrical stimulation to enable men and women with SCI to empty their bladders on demand, thereby improving their quality of life, decreasing reliance on catheters, and possibly reducing the occurrence of urinary tract infections.

METHODS

The patient was a 38-year-old woman with a C6 ASIA A SCI secondary to a motor vehicle crash 4 years prior. She

Figure 1. Detrusor pressure in response to electrical stimulation (bar) of the urethra. Electrical stimulation of the distal urethra at 35 mA, 20 Hz, evoked a bladder contraction, which generated some voiding, but the bladder neck was occluded by a Foley balloon and the voided volume was not recorded. Bladder volume prior to stimulation was approximately 90% of the volume threshold for distention-evoked contractions (V_{th}). Peak detrusor pressure increase evoked by stimulation was approximately 70 cmH₂O.

demonstrated neurogenic detrusor overactivity on urodynamics and managed her bladder with clean intermittent catheterization and oxybutynin.

The research study followed the guidelines of the Declaration of Helsinki and was approved by the institutional review board. After the patient provided informed consent, she discontinued oxybutynin 2 days prior to urodynamic testing. Urodynamic testing was performed with a custom 12F balloon catheter (uncoated silicone Foley catheter with 5-mL balloon, Bard Inc,

Figure 2. Detrusor pressure in response to urethral stimulation at different bladder volumes. Electrical stimulation of the distal urethra did not evoke a bladder contraction when the bladder was filled to 50% of V_{th} (A), but stimulation did evoke a contraction when the bladder was filled to 70% of V_{th} (B). Stimulus amplitude was 22 mA and frequency was 20 Hz. Bladder contraction generated some voiding, but the voided volume was not recorded. Peak detrusor pressure increase evoked by stimulation was approximately 75 cmH₂O.

Covington, GA) mounted with ring-shaped electrodes (304 stainless steel, 3 mm wide) at 1, 3, and 5 cm from the balloon corresponding to the bladder neck, midurethra, and distal urethra. The inflated balloon was placed against the bladder neck to stabilize the catheter electrodes in place along the urethra. Placement of the balloon in the bladder neck may have limited the potential for emptying during contractions and may have increased voiding pressure by obstructing the bladder outlet. Bladder pressure was recorded via the custom catheter, and abdominal pressure was recorded via a 10F balloon catheter (Bard Inc) placed in the rectum. Abdominal pressure was subtracted from bladder pressure to obtain detrusor pressure. Data were recorded and stored on a urodynamic monitoring system (Laborie Aquarius TT, Triton, Toronto, Canada).

Prior to the procedure, the patient was catheterized and urinary tract infection was excluded via dipstick urinalysis. The leukocyte, esterase, and nitrate indicators were negative. The custom electrode catheter was placed under sterile conditions and the bladder was filled at a rate of 25 mL/minute until a distention-evoked bladder contraction occurred; this volume was labeled threshold (V_{th}). The bladder was then drained and filled in increments, expressed as a percentage of V_{th} , to begin the stimulation trials. The urethra was stimulated over a range of parameters (location, amplitude, and frequency) to determine whether electrical stimulation could evoke a bladder contraction. Electrical stimulation was generated by a regulated current stimulator (SMP-plus, Medi-Stim Inc, Wabasha, MN). A 2-inch round self-adhering surface electrode (Rehabicare, New Brighton, MN) placed on the hip of the patient served as the return electrode.

For each stimulation trial, 1 of the 3 ring electrodes in the urethra was chosen as the active contact. Stimulation was applied in trains of asymmetric charge-balanced biphasic pulses with cathodic pulse width of 200 μ s. Stimulation frequency was varied from 10 to 40 Hz, and stimulation amplitude was varied from 10 to 60 mA. The duration of the stimulus trains was 30 to 120 seconds. The patient returned after the first day of urodynamic testing for a second visit approximately 3 months later so that testing could be continued and the responses to additional stimulus parameters recorded. Each visit lasted approximately 2.5 hours. No adverse events were reported.

FINDINGS

Electrical stimulation of both the distal urethra and midurethra evoked bladder contractions when the bladder volume was equal to 90% of V_{th} (Figure 1). When the bladder contained 50% of V_{th} (45 mL), stimulation (20 Hz, 22 mA) of the distal urethra did not evoke a bladder contraction, but the same stimulus parameters did generate a contraction when the volume was increased to 70% of V_{th} (65 mL) (Figure 2). Similarly,

Figure 3. Detrusor pressure in response to urethral stimulation at different stimulus amplitudes. Electrical stimulation of the midurethra at 12 mA did not evoke a bladder contraction (A), but stimulation at 15 mA evoked a substantial increase in detrusor pressure (B). Bladder contraction generated some voiding, but the volume voided was not recorded. Bladder volume was 70% of V_{th} at the beginning of each stimulation trial, and stimulation frequency was 20 Hz. Peak detrusor pressure increase evoked by stimulation was approximately 85 cmH₂O.

stimulation of the mid urethra evoked bladder contractions only when the bladder was filled to at least 70% of V_{th} . These data indicated that the bladder had to be filled to a minimum volume of approximately 70% of V_{th} before stimulation could evoke a bladder contraction.

Setting bladder volume to 70% of V_{th} and varying stimulus amplitude indicated that 15 mA was the minimum current amplitude observed to evoke a bladder contraction. Stimulation at the same parameters (20 Hz, 70% of V_{th}) but with amplitudes of 12 mA or less did not evoke contractions (Figure 3). Urethral stimulation evoked peak bladder detrusor pressures of 70 to 85 cmH₂O. Stimulation of the distal urethra provided the most consistent response across different amplitudes, and 22 mA was the lowest amplitude (at 20 Hz) that most consistently evoked bladder contractions (Table 1).

Table 1. Responses of Bladder Detrusor Pressure to Electrical Stimulation of the Distal Urethra when Bladder Volume Was Filled to at Least 70% of V_{th}

Stimulation Amplitude	Stimulation Frequency					
	10 Hz	15 Hz	20 Hz	25 Hz	30 Hz	40 Hz
60 mA			(+) v2			(-) v2
50 mA		(+) v2	(+) v2	(-) v2		
35 mA			(++) v2 (++) v1			(-) v2
22 mA	(-) v2		(+) v2		(-) v2	(+) v2
15 mA			(-) v1			(+) v2
12 mA			(-) v1			
10 mA						(-) v2

Bladder response is indicated by the symbol: excitatory (+) or nonexcitatory (–), followed by the visit number: v1 (visit number 1) or v2 (visit number 2). If a parameter set was tested twice and evoked excitatory responses both times, 2 symbols appear (++). Stimulation at bladder volumes of less than 70% of V_{th} failed to evoke a bladder contraction.

DISCUSSION

The present case study reports the first time bladder contractions were evoked in a woman with SCI using electrical stimulation of the urethra. These data suggest that an excitatory urethra-to-bladder spinal reflex exists in a woman with SCI and that an instrument as simple and minimally invasive as a standard Foley catheter mounted with ring electrodes may be used to investigate the excitatory urethra-to-bladder reflex during urodynamic testing.

The present study complements previous studies in men with SCI in which electrical stimulation of the urethra or the pudendal nerve evoked bladder contractions (11,12). The present data are also consistent with electrical stimulation of pudendal urethral afferents evoking bladder contractions in male cats after acute spinal transection and in female cats after chronic spinal transection (5–8,10,13).

Electrical stimulation of the urethra may be activating the same augmenting reflex that is evoked by fluid flow along the urethra. The urethra-to-bladder reflex was initially observed by Barrington (14,15) in cats and later documented in humans (16). Urethral fluid flow is known to evoke a bladder contraction only when the bladder contains a minimum volume, approximately 65% of the volume threshold (V_{th}) for distention-evoked contractions (17). This minimum volume matches well with the volume (70% of V_{th}) required to evoke a bladder contraction in the woman with SCI in the present study and falls within the range (60%–78%) published for men with SCI in clinical and preclinical studies (7,9,12).

The mechanism of evoking contractions may be by direct stimulation or by release of inhibition (rebound), a mechanism thought to operate during magnetic stimulation of sacral nerve roots in previous studies (18,19).

CONCLUSION

Future study is needed to compare bladder responses to stimulus trains of various durations to determine whether contractions are evoked by excitation or by release of inhibition. Whether contractions are evoked by excitation or by release of inhibition, the ability to evoke bladder contractions via urethral stimulation holds promise for eventual restoration of bladder emptying, and the clinical utility will ultimately be determined by how efficiently the contractions can empty the bladder.

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