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INHIBITION OF BLADDER OVERACTIVITY BY TRANSCUTANEOUS STIMULATION TARGETING THE PUDENDAL NERVE IN CATS

Hypothesis / aims of study

Our previous studies using chronic spinal cord injured cats under anesthesia have shown that electrical stimulation of the pudendal nerve at different stimulation frequencies using an implanted cuff electrode could either inhibit or excite the bladder. The goal of current study was to further investigate a non-invasive neurostimulation method to inhibit bladder overactivity induced by acetic acid irritation. This preclinical study is aimed at developing a noninvasive stimulation method to treat neurogenic bladder overactivity.

Study design, materials and methods

The Selective Nerve Stimulation (SNS, known as "Project SyNapSe") device provides non-invasive, transcutaneous neurostimulation through a controlled, amplitude-modulated waveform. This carrier waveform is designed to be of sufficient frequency to overcome tissue impedance. The pulse envelope contains specific pulse width, amplitude, and shape information designed to stimulate specific nerves. In the present study, the SNS electrical stimulation method was used to activate the pudendal nerve of normal female cats (n=12) non-invasively, under α-chloralose anesthesia, to produce either an inhibitory or excitatory bladder response. A pair of self-adhesive surface pad electrodes was attached to the skin area between the base of the tail and the sciatic notch. A high-frequency sinusoidal waveform, modulated by a low-frequency electrical pulse, was delivered to the skin via the pad electrodes at different pulse frequencies (5-40 Hz) and intensities (7-19V). A double lumen catheter was inserted through the urethra into the bladder to monitor the bladder pressure and infuse (0.5–3 mL/min) saline or 0.25% acetic acid (AA). The ureters were cut and drained externally.

Results

During cystometrogram (CMG), infusion of 0.25% AA significantly decreased bladder capacity to 28.8±5.9% of the bladder capacity measured during saline infusion. Transcutaneous stimulation at 5 Hz, 7 Hz, and 10 Hz inhibited AA induced bladder overactivity and significantly increased the bladder capacity to 61.8±9.9%, 51.3±14.5%, 53.6±14.9% respectively of the saline control capacity, whereas stimulation at 20-40 Hz had no effect. Under isovolumetric conditions at a bladder volume about 130-160% of the bladder capacity measured during AA infusion, transcutaneous stimulation at frequencies of 5-40 Hz significantly suppressed the irritation induced rhythmic bladder contractions, reduced the area under bladder pressure curve, and decreased the frequency of bladder contractions. However, the amplitude of rhythmic bladder contractions was only significantly decreased at stimulation frequency of 5-20 Hz. The excitatory effect of transcutaneous stimulation was dependent on bladder volume and stimulation frequency. Large amplitude (>25 cm H_2O) bladder contractions could only be induced at 20-30 Hz when bladder volume was above the AA control bladder capacity.

Interpretation of results

During AA irritation the transcutaneous stimulation at 5-10 Hz almost doubled the bladder capacity (increased from 30% to 60%). However, the increased bladder capacity was only about half of the bladder capacity measured during saline infusion. This result indicated that the transcutaneous stimulation only partially inhibited the irritation induced, C-fiber mediated micturition reflex. Otherwise, the bladder capacity should be fully restored to that measured during saline infusion without AA irritation. This partially inhibitory effect could be due to the efficacy of the transcutaneous stimulation method. The stimulation intensity was limited to avoid activation of the sciatic nerve, which might result in a partial activation of the pudendal nerve. Further studies employing direct stimulation of the pudendal nerve are needed in order to determine whether pudendal nerve afferent input can completely inhibit the C-fiber mediated, pelvic-to-pelvic micturition reflex. Transcutaneous stimulation at 20-40 Hz significantly suppressed the rhythmic bladder activity under isovolumetric conditions during AA irritation. However, the same stimulation frequency failed to significantly increase the bladder capacity during AA infusion, indicating a weak inhibitory effect on bladder overactivity at frequencies between 20 and 40 Hz. Stimulation at 30-40 Hz also failed to significantly reduce the contraction amplitude during rhythmic bladder contractions, further indicating a weak inhibitory effect. The excitatory effect at frequencies between 20-30 Hz was also weak, since it could only induce small amplitude (<25 cm H_2O) bladder contractions at a bladder volume below bladder capacity. In contrast to the high frequency range (20-40 Hz), the low frequency range (5-10 Hz) exhibited only inhibitory effect without excitation, indicating that the transcutaneous stimulation at a low frequency might be more effective than a high frequency to treat neurogenic bladder overactivity in clinical applications.

Concluding message

This preclinical study demonstrated the possibility of inhibiting neurogenic bladder overactivity by a noninvasive electrical stimulation method using skin surface electrode attached to the lower back of the body to target the pudendal nerve. Previous studies targeting the pudendal nerve to inhibit bladder activity are either inconvenient for the patients or not suitable for chronic use. Development of a noninvasive stimulation method targeting the pudendal nerve at a location convenient for the patients will further promote the application of neuromodulation for treatment of neurogenic bladder overactivity, urgency, frequency, and incontinence.

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