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RANDOMIZED, DOUBLE-BLIND STUDY OF ELECTRICAL STIMULATION FOR URINARY INCONTINENCE DUE TO DETRUSOR OVERACTIVITY

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ABSTRACT

Objectives. To evaluate the usefulness of electrical stimulation for urinary incontinence due to detrusor overactivity in a randomized, double-blind manner.

Methods. Sixty-eight patients (29 men, 39 women, 70.0 ± 11.2 years) were studied. Detrusor overactivity was urodynamically defined as involuntary detrusor contractions of more than 15 cm H_2O during the filling phase. Ten-hertz square waves of 1-ms pulse duration were used. A vaginal electrode was used in the women and an anal or surface electrode in the men. The stimulation was given for 15 minutes twice daily for 4 weeks. The efficacy was evaluated on the basis of a frequency/volume chart and urodynamic study before and after treatment.

Results. Thirty-two patients in the active group and 28 in the sham group completed the study. The patient impressions were very good or good in 59% and 39% of the active and the sham group, respectively ($P = 0.0354$). On the cystometrogram, the bladder capacity at the first desire to void and the maximum desire to void increased significantly ($P = 0.0104$ and $P = 0.0046$, respectively) in the active group, but not in the sham group. Seven patients in the active group and 1 patient in the sham group were cured ($P = 0.0324$); 26 patients (81.3%) in the active group and 9 (32.1%) in the sham group improved ($P = 0.0001$). Of 17 patients in the active group, 13 remained cured or improved for an average of 8.4 months after completion of the 4-week treatment; in the sham group, 3 of 6 patients were cured or improved for an average of 4.7 months after completion of the 4-week treatment.

Conclusions. Electrical stimulation was useful in treating urinary incontinence due to detrusor overactivity. UROLOGY **55:** 353–357, 2000. © 2000, Elsevier Science Inc.

Electrical stimulation has been reported to be safe and effective for urinary incontinence. Success rates for urge incontinence have been reported to range from 50% to 90%.[1–4] The frequencies of 5 to 20 Hz with a pulse duration of 1 to 5 ms have been reported to be optimal for the inhibition of detrusor contraction.[5–9] Electrical stimulation has been performed in three different ways: percutaneously using a needle or surface electrode, intra-anally using an anal electrode, and intravaginally using a vaginal plug. All have been reported to result in sufficient inhibition of detrusor overactivity.[1,3,7,8,10] However, some patients refuse anal electrodes because of the discomfort at the insertion of the plug.

The present randomized, placebo-controlled, double-blind study using an active or sham device was designed to verify the usefulness of electrical stimulation for urge incontinence. For the double-blind trial, treatment twice daily for 4 weeks has been reported to be enough to evaluate the clinical results.[2,4,11] Consequently, the present study was designed to perform electrical stimulation twice daily for 4 weeks, with an anal or a surface electrode in male patients and a vaginal electrode in female patients. Square waves with a pulse width of 1 ms and a frequency of 10 Hz were used for stimulation.

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MATERIAL AND METHODS

The study included 68 patients with urinary incontinence due to detrusor overactivity (29 men and 39 women; mean age 70.0 years, range 35 to 87).

No patients had been taking anticholinergics or tricyclic depressants and none had been treated by pelvic floor exercise, bladder training, or pelvic surgery before entry into the study. Pretreatment urinalysis and urine cytologic examination revealed no abnormality in any of our patients. No associated pelvic organ prolapse was present in the female patients. Neurologic examinations, including perineal sensation, tonus of the anal sphincter, anal reflex and bulbocavernosus reflex, and spinal or cranial computed tomography and magnetic resonance imaging were performed to detect underlying diseases of neurogenic bladder. The presence or absence of bladder outlet obstruction such as benign prostatic hypertrophy was examined by ultrasound of the prostate and voiding cystourethrography. The procedures were approved by the local ethics committee, and written informed consent was obtained from each patient before entry into the study.

Patients were randomly assigned to either the active or the sham device. The sham device was identical to the active device in appearance but with no stimulus output. The device had five LEDs to indicate the stimulation intensity, which was adjusted by turning the knob at the top of the device. To ensure maximum blindness of the study, neither doctors, nurses, nor patients knew which device was active or sham, except for the controller who kept the key code. The patients were informed that two different devices would be used: one that would give some irritancy and another that would be free of irritancy. Alternating pulses of 10-Hz square waves of 1-ms pulse duration and a maximum output current of 60 mA were used for active electrical stimulation. Stimulation up to the maximum tolerable level was given. A surface electrode or an anal plug was used in the men and a vaginal plug in the women. The surface electrode was placed onto the dorsal part of the penis. The electrode plug for anal use was bullet-shaped, and the vaginal plug was cylinder-formed with ring-formed electrodes. The stimulation was given for 15 minutes twice daily for 4 weeks.

Patients recorded the number of voids, number of leaks, and number of pad changes on the frequency/volume chart and their impressions, degrees of urgency, and quality-of-life score on the questionnaire chart. The degree of urgency was scored as 0 = none, 1 = slight, 2 = moderate, and 3 = very much and quality of life as 0 = delighted, 1 = mostly satisfied, 2 = dissatisfied, and 3 = mostly dissatisfied or unhappy. The patient impressions as subjective assessments obtained from the questionnaires were ranked as "very good," "good," "fair," or "not good."

Urodynamic studies were performed before and after the 4-week treatment. An 8F double-lumen catheter was inserted transurethrally and a water cystometrogram was recorded at an infusion rate of 50 mL/min in the supine position; simultaneously, the rectal pressure was monitored with a balloon catheter and subtracted from the intravesical pressure. Detrusor overactivity was defined as involuntary detrusor contractions of more than 15 cm H_2O during the filling phase. Changes in bladder capacity of at least 50 mL due to the electrical stimulation was defined as significant inhibition of the bladder.[5]

The efficacy of the electrical stimulation therapy was judged on the basis of the records in the frequency/volume chart and the cystometric results: "cured" if the patient had no incontinence on the frequency/volume chart and no detrusor overactivity according to cystometry and "improved" if the frequency of the incontinence decreased by more than 50% compared with the baseline level or the cystometric capacity increased by more than 50 mL.

After the 4-week treatment, patients who were cured or improved were followed up monthly on the basis of the records in the frequency/volume chart to evaluate post-stimulation effects. If the patient relapsed, the stimulation was repeated periodically in the same way using the same device until continence was regained.

Statistical Analysis

All results are expressed as the mean ± SD. The Wilcoxon signed rank-sum test was used for intragroup differences. Student's *t* test, Fisher's exact probability test, and the Mann-Whitney *U* test were used to evaluate the intergroup differences and the effects of the therapy. *P* values of less than 0.05 were considered statistically significant.

RESULTS

Thirty-seven patients were assigned to the active group and 31 to the sham group. The two treatment groups were well matched, except for the age distribution (Table I). Four patients (3 in the active group and 1 in the sham group) did not return after the first visit, and 4 patients (2 in the active and 2 in the sham group) discontinued because of disagreeable feelings or vaginal pain. Sixty patients completed the study.

According to the records in the frequency/volume chart, urinary frequency and nocturia significantly decreased in the active group ($P = 0.0079$ and $P = 0.0007$, respectively), and a significant intergroup difference ($P = 0.0298$) was noted with regard to nocturia. The number of leaks significantly decreased ($P = 0.0002$) in the active group, but not in the sham group ($P = 0.2761$) after the therapy. An intergroup difference ($P = 0.0015$) in frequency of incontinence was evident (Fig. 1).

The daily frequency of pad changes before and after the treatment was 1.9 ± 1.7 and 0.8 ± 1.2 times ($P = 0.0010$), respectively, in the active group and 1.4 ± 2.0 and 1.1 ± 2.0 times ($P = 0.0431$), respectively, in the sham group. An intergroup difference was noted in favor of the active group ($P = 0.0640$). The score of urgency before and after the treatment was 2.3 ± 0.7 and 1.7 ± 0.7 ($P = 0.0007$), respectively, in the active group and 2.2 ± 0.8 and 2.0 ± 0.8 ($P = 0.0630$), respectively, in the sham group.

The quality-of-life score before and after the treatment was 2.4 ± 0.7 and 1.6 ± 0.7 ($P < 0.0001$), respectively, in the active group and 2.6 ± 0.8 and 2.2 ± 0.9 ($P = 0.0051$), respectively, in the sham group. A significant intergroup difference ($P = 0.0455$) was noted in favor of the active group.

The average and maximum flow rates were normal, and the residual urine volume was less than 50 mL in all subjects before treatment; no changes occurred after treatment. Two patients in the sham

TABLE I. *Patient characteristics*

	Active Group (n = 37)	Sham Group (n = 31)	Total (n = 68)	*P* Value
Sex				
Male	14	15	29	0.4631*
Female	23	16	39	
Urge incontinence	33	27	60	Urge vs. reflex 0.6553*
Reflex incontinence	2	3	5	Urge vs. urge + stress >0.9999*
Urge and mild stress incontinence	2	1	3	
Age (yr)	67.5 ± 12.7	73.0 ± 8.7	70.0 ± 11.2	0.0463†
Body weight (kg)	53.4 ± 8.7	50.6 ± 9.6	52.0 ± 10.0	0.2287†
Height (cm)	151.6 ± 9.6	152.4 ± 9.1	152.1 ± 8.9	0.7632†
Duration of disease (mo)	56.2 ± 61.9	55.5 ± 95.4	55.9 ± 78.6	0.7308†
Severity				
Mild	28	24	52	1.0000*
Severe	9	7	16	
Underlying disorders				
Male				
Neurogenic bladder	8	10	18	0.7104*
Unstable‡	6	5	11	
Female				
Neurogenic bladder	11	10	18	0.3487*
Idiopathic§	13	6	21	
Electrodes used				
Surface	8	11	19	Surface vs. anal 0.4497*
Anal	6	4	10	Surface vs. vaginal 0.4076*
Vaginal	23	16	39	Anal vs. vaginal 0.9999*

* *Fisher's exact probability test.*
† *Student's* t *test.*
‡ *Unstable bladder due to mild benign prostatic hyperplasia or postprostatectomy (transurethral resection of the prostate or radical prostatectomy) incontinence.*
§ *Idiopathic detrusor instability.*

group refused to undergo the postoperative urodynamic study. On the cystometrogram, the bladder capacity at the first desire to void and the maximum cystometric capacity increased significantly ($P = 0.0104$ and $P = 0.0046$, respectively) in the active group, but not in the sham group ($P = 0.3395$ and $P = 0.5338$, respectively). Significant intergroup differences in bladder capacity at the first desire to void and the maximum cystometric capacity were noted in favor of the active group (Table II).

Detrusor overactivity disappeared in 8 patients (25%) and improved in 20 patients (62.5%) in the active group; it also disappeared in 2 patients (7.7%) and improved in 7 patients (26.9%) in the sham group. A significant difference ($P = 0.0037$) was found with regard to the number of patients who demonstrated improvement in detrusor overactivity in favor of the active group.

The patient impression was "very good or good" in 19 (59.4%) and "fair or not good" in 13 (40.6%) patients of the active group and "very good or good" in 11 (39.3%) and "fair or not good" in 17 (60.7%) patients of the sham group ($P = 0.0354$).

Seven patients (21.9%) in the active group and 1 patient (3.6%) in the sham group were cured, and 26 patients (81.3%) in the active group and 9 (32.1%) in the sham group were improved. The number of cured and improved patients was significantly higher in the active group than in the sham group ($P = 0.0324$ and $P = 0.0001$, respectively). A significant difference in favor of the active group was found when the patients were divided into two subgroups according to sex ($P = 0.0213$ for men and $P = 0.0091$ for women) and also when they were divided according to those younger than 60 and those 60 years old or older ($P = 0.0050$ for the former and $P = 0.0086$ for the latter).

Adverse Effects

Adverse effects were noted in 2 (5.4%) of 37 patients of the active group (vaginal pain in 1 and fecal incontinence in 1), and in 2 (6.5%) of 31 patients of the sham group (disagreeable feeling).

Post-Stimulation Effects

Seventeen of 26 patients in the active group who were cured or improved were followed up monthly for an average of 8.9 months (range 3 to 26) after the treatment. Seven patients (41.2%) had continence for 3 to 12 months (mean 8.4) without treatment, and the remaining 10 patients had a relapse of incontinence 1 to 5 months (mean 2.0) after treatment. Six of these 10 patients achieved satis-

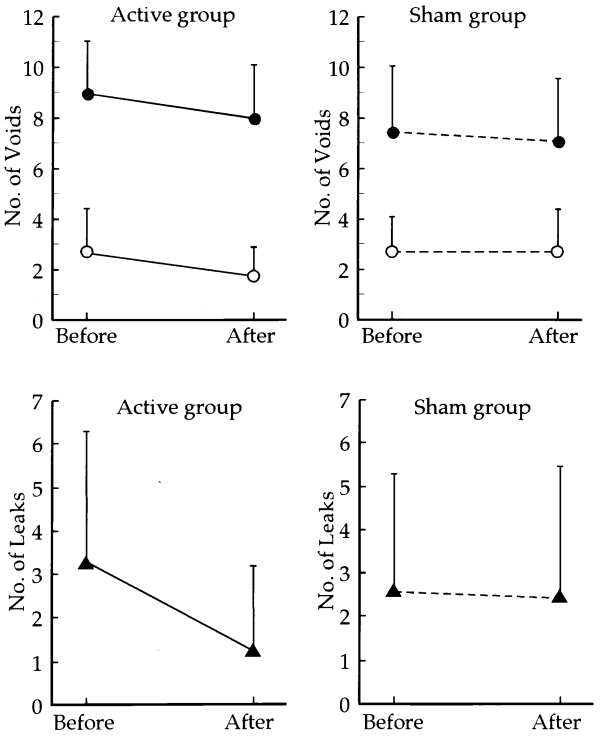

FIGURE 1. *Changes in number of daytime and nighttime voids and in number of episodes of leakage per day. Solid line with black circles indicates number of daytime voids in the active group; solid line with white circles indicates number of nighttime voids in the active group; dashed line with black circles indicates number of daytime voids in the sham group; dashed line with white circles indicates number of nighttime voids in the sham group; solid line with black triangles indicates number of leaks in the active group; dashed line with black triangles indicates number of leaks in the sham group.*

factory control by periodical restimulation. The remaining 4 patients were prescribed anticholinergics at their request. In the sham group, 6 of the 9 improved patients were followed up for 1 to 24 months (mean 9.8) after treatment. Three patients were in satisfactory status without treatment for 1 to 8 months (mean 4.7). The remaining 3 patients had recurrence of incontinence at 1 month after treatment, but it was not improved by restimulation with the same sham device.

COMMENT

The mechanism of electrical stimulation for detrusor inhibition is the reflex inhibition of pelvic efferents or activation of hypogastric efferents through stimulation of the afferent input in the pudendal or sacral root.[6,12,13] Low-frequency pudendal nerve stimulation has been reported to activate the spinal interneurons that release inhibitory neurotransmitters, such as opioid peptides (endorphin/enkephalin), glycine, or gamma-aminobutyric acid[10,14] and also has been reported to increase beta-adrenergic activity in the detrusor muscle.[15]

Few controlled studies on the electrical stimulation for urge incontinence have been done. Bower *et al.*[16] reported an inhibition of detrusor activity using active surface electrical stimulation, but not with the sham stimulation. However, their study was designed only to test the acute suppression of detrusor overactivity. Brubaker *et al.*[17] reported that detrusor instability became stable in 49% of the women with detrusor instability using an active device, but no changes were noted with the sham device. Their patients included those with stress and mixed incontinence. They found no significant difference with respect to the quality of life, and the urinary diaries were not reliable because the records were incomplete. Abel *et al.*[18] reported a significantly better subjective improvement in the electrical stimulation treatment group than the placebo group, but no difference in the objective outcomes between the two groups was found. Taking into consideration the contents of these studies, our present work may be the first randomized clinical study to prove subjectively and objectively the efficacy of electrical stimulation in incontinence due to detrusor overactivity.

A controlled study on physical treatment is very difficult to achieve because the use of a nonfunctioning stimulator as a control is too easy for the patient to detect.[11,19] Although our data demonstrated the superiority of the active treatment to the sham treatment subjectively and objectively, the subjective data (patient impression) seem to be less reliable. Therefore, the therapeutic efficacy of electrical stimulation was judged objectively, from the occurrence of leakage in the frequency/volume chart and cystometric data.

Apart from the significant improvement in the active group, some improvement also occurred in the sham group. This placebo effect may be attributed to the fact that patients were completing micturition diaries and were closely monitored, which may have acted as a form of bladder training.[20] Although there was a statistically significant age difference between the active and sham group, the age difference did not seem to affect the efficacy, as a significant superiority in preference of the active group was found when the patients were divided into those younger than 60 years and those 60 years old or older.

Fall[3] reported that of 40 patients with urinary incontinence treated with electrical stimulation, 45% remained free of symptoms after withdrawal of treatment. The cause of re-education was considered to be a central adaptation, with improvement of subconscious inhibitory mechanisms or decrease in facilitatory activity, or both.[9] In our

TABLE II. *Changes in urodynamic parameters*

	Active Group (n = 32)		Sham Group (n = 26)		*P*
	Before	After	Before	After	Value*
Bladder capacity at first desire to void (mL)	148.8 ± 74.8	174.2 ± 83.1	147.3 ± 59.3	130.0 ± 69.9	0.0316
Maximum cystometric capacity (mL)	234.4 ± 124.8	285.0 ± 143.4	202.0 ± 95.4	182.9 ± 99.0	0.0186
Detrusor pressure at maximum sensation (cm H_2O)	37.4 ± 16.8	34.6 ± 12.5	33.6 ± 13.6	34.8 ± 13.6	0.9298
Amplitude of detrusor overactivity (cm H_2O)	51.1 ± 33.6	39.1 ± 36.6	53.2 ± 33.8	50.9 ± 29.8	0.0726
Bladder compliance at maximum sensation (mL/cm H_2O)	21.3 ± 16.7	27.8 ± 24.1	22.8 ± 8.3	31.6 ± 35.7	0.8825

** Intergroup difference; Mann-Whitney U test.*

present study, 41% of 17 patients treated with the active device remained cured for 8.9 months on average after stimulation, and 35% of patients relapsed but could achieve control with periodic electrical stimulation. The results of this follow-up study suggest that a prolonged post-stimulation effect was obtained as a result of the electrical stimulation.

CONCLUSIONS

This study verified the superiority of the active treatment compared with the sham treatment and proved the efficacy of electrical stimulation for the treatment of urinary incontinence due to detrusor overactivity.

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