Transvaginal electrical stimulation for female urinary incontinence

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OBJECTIVE: Our purpose was to determine the objective and subjective efficacy of transvaginal electrical stimulation for treatment of common forms of urinary incontinence in women.
STUDY DESIGN: A prospective, double-blind, randomized clinical trial included 121 women with either urinary incontinence caused by detrusor instability or genuine stress incontinence, or both (mixed incontinence). Participants used the assigned device for 8 weeks. Identical preintervention and postintervention assessment included multichannel urodynamic testing, quality-of-life scale, and urinary diaries.
RESULTS: A total of 121 women completed this study at four North American urogynecology centers. Detrusor instability was cured (stable on provocative cystometry) in 49% of women with detrusor instability who used an active electrical device ($p = 0.0004$, McNemar's test), whereas there was no statistically significant change in the percentage with detrusor instability in the sham device group. There was no statistically significant difference between the preintervention and postintervention rates of genuine stress incontinence for either the active device group or the sham device group.
CONCLUSION: This form of transvaginal electrical stimulation may be effective for treatment of detrusor overactivity, with or without genuine stress incontinence. (Am J Obstet Gynecol 1997;177:536-40.)

Key words: Electrical stimulation, detrusor overactivity, urinary incontinence

Various forms of electrical stimulation have been used in the treatment of female urinary incontinence. Transvaginal stimulation with a removable electrode has been in clinical use in Europe and North America for three decades. Many early publications reported efficacy without the benefit of a control population.[1-3] Two randomized studies have reported the usefulness of transvaginal electrical stimulation.[4, 5] This type of therapy is rarely covered by third-party payers, in part because of a belief that this form of therapy is experimental. This study compares the efficacy of a single method of transvaginal electrical stimulation with that of a sham device in ambulatory women with commonly found causes of urinary incontinence.

Material and methods

Women who have symptoms and urodynamic evidence of either genuine stress incontinence or detrusor overactivity, or both, were sought as study participants. Four centers participated in this investigation: Rush-Presbyterian–St. Luke's Medical Center, Chicago; Methodist Hospital, Indianapolis; Greater Baltimore Medical Center; and the Oregon Health Science University, Portland.

The standardized intake assessment included a comprehensive urogynecologic history and physical, multichannel urodynamic testing, urinary diary, and assessment of quality of life. The method of urodynamic testing (Table I) was standardized among the four participating institutions. Either detrusor instability or genuine stress incontinence, or both, were defined as objectively cured if the previously documented abnormality was absent on the postintervention study. Women were excluded according to the criteria in Table II. Each participant met the criteria for study inclusion and gave verbal and written consent, in compliance with each local institutional review board. Once enrolled by a physician investigator, subjects were stratified into three distinct groups according to the urodynamic diagnosis, as follows: pure genuine stress incontinence, pure detrusor instability, or mixed incontinence. Within these groups, participants were randomized to one of two devices. Randomization schemes stratified by incontinence type were constructed for all sites by a statistician, using computer-generated random numbers, and used for stratified randomization. The study nurse at each site was responsible for carrying out the random assignment of patients in accordance with the randomization scheme

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Table I. Urodynamic testing

Subjectively full stress test
Spontaneous uroflowmetry
Residual urine assessment
Filling urethrocystometry
• Infusion of room-temperature water at 100 ml/min
• Patient seated in birthing chair
• Provocative maneuvers at maximum capacity
• Repeated in standing position if sitting study normal
Urethral pressure profiles
• Resting
• Cough
Instrumented voiding study

Table II. Exclusion criteria

Urinary incontinence other than genuine stress incontinence, detrusor instability, or mixed incontinence
Age <25 yr
Leakage episodes ≤3/wk
Inadequate genitourinary estrogen (minimum 3 mo replacement)
Inadequate cognitive ability (investigator judgment)
Infected urine
Anatomic defect that precluded use of device
Postvoid residual >100 ml
Implanted electric device
Genitourinary surgery ≤6 mo previously
Medication alteration ≤3 mo previously
Anticipated geographic relocation during study

for that site. The transvaginal electric stimulation group (stimulation group) used the InCare Microgyn II. The selected electric parameters included a frequency of 20 Hz, a 2-second–4-second work-rest cycle, and a pulse width of 0.1 μsecond. The bipolar square wave could be delivered over a range of 0 to 100 mA. The InCare Division (Hollister, Inc., Libertyville, Ill.) provided the study units without cost to the investigators or participants. Additional industry support was limited to $2000 for data entry by the independent data managers. The subjects were not paid for their participation. The control group (sham group) received a device that was externally identical, including the LED (light-emitting diode)–lighted display on the front of the unit. Within the vaginal probe, however, a single wire had been disconnected before shipping so that no electrical energy was supplied. The LED light on the handheld unit remained lit, and patients with a sham device were told to increase this to a standardized setting. Stimulation subjects were instructed to stimulate to the maximum tolerable motor response. The consent form was worded to remove expectations regarding sensory input by stating that we were studying a range of stimulation intensities, from 0 to 100 mA.

The study nurse at each site was aware of the difference in probes; however, the physician investigators were masked as to the type of vaginal probe provided to each participant.

After a 1-week baseline assessment period, treatment began with use of the assigned device for 20 minutes twice daily. Study nurses provided telephone contact with patients at the second and sixth weeks of treatment. An office visit at 4 weeks was used to assess compliance by reading an internal compliance meter of the machine. The stimulator stores the time and amperage during use. This is downloaded to an office unit to determine patient compliance. Treatment continued until participants had completed 8 weeks with the assigned device. At this point a posttreatment assessment, which was identical to the intake assessment, was done. The final subjective assessment occurred after a 2-week observation period.

This study used a disorder-specific quality-of-life instrument that had been tested previously in a small pilot series of patients. The 41-question document had been modified from a cancer-specific quality-of-life tool and included five specific domains (physical, emotional, functional, social, and physician relationship), in addition to incontinence-specific questions. Quality-of-life assessment was done four times, as follows: at enrollment, at the start of treatment, at the completion of treatment, and at the end of the study.

The urinary diary was a standardized instrument that had been successfully used in previous incontinence clinical trials.[6] Diurnal frequency and nocturnal frequency were recorded, as well as the number of incontinent episodes and pads used. The urinary diary was collected at the same time points as the quality-of-life instrument.

Data were sent to a centralized data manager for entry. After completion of data entry, an independent statistician provided data analysis. At no time were the data made available to the maker of the device. Groups were compared with respect to nominal variables by means of the χ^2 test of association. The nonparametric Mann-Whitney test was done to compare groups with respect to variables that were at least ordinal. To compare preintervention and postintervention rates, the McNemar test was used.

Results

A total of 148 women were enrolled, 18% of whom withdrew from the study, leaving a total of 121 participants who completed the study. There was no statistically significant difference between the treatment groups with respect to withdrawal rates: 21% for the sham group and 14% for the stimulation group ($p = 0.27$, χ^2 test of association). Subjects who withdrew from the study were excluded from all further analyses, because follow-up data were not available for these subjects. Withdrawal rates varied by site, and the difference was statistically significant: Rush 19%, Methodist 37%, Baltimore 6%, and Portland 7% ($p = 0.0008$, χ^2 test of association).

Table III. Study population description

Background variable	*Sham*	*Electric stimulation*	*Significance (sham vs electric stimulation)*
Age (yr)	57.7 ± 12.4	56.0 ± 11.9	p = 0.44, pooled-variable t test
Weight (lb)	158.9 ± 34.5	166.7 ± 41.0	p = 0.55, Mann-Whitney test
Leakage protection	88%	93%	p = 0.31, χ^2 test
Previous treatment (not self-treatment) for incontinence	56%	49%	p = 0.45, χ^2 test
Previous surgery for incontinence	36%	35%	p = 0.94, χ^2 test
Previous medical treatment for incontinence	23%	27%	p = 0.62, χ^2 test
Previous exercise treatment for incontinence	39%	39%	p = 1, χ^2 test
Previous self-treatment for incontinence	55%	67%	p = 0.20, χ^2 test
Symptoms of stress incontinence	90%	92%	p = 0.71, χ^2 test
Symptoms of urge incontinence	75%	70%	p = 0.62, χ^2 test
Hormone replacement therapy (postmenopausal only)	87%	87%	p = 0.96, χ^2 test
Anticholinergicor spasmolytic use	14%	14%	p = 0.93, χ^2 test
Previous genitourinary surgery	85%	88%	p = 0.57, χ^2 test
Vaginal delivery	90%	90%	p = 0.95, χ^2 test
No. of vaginal deliveries	2.7 ± 1.6	2.6 ± 1.1	p = 0.69, Mann-Whitney test
Grade of anterior vagina or cystocele prolapse (grade 1-4)	1.0 ± 0.8	1.1 ± 0.9	p = 0.51, Mann-Whitney test
Grade of uterus or vault prolapse (grade 1-4)	0.2 ± 0.5	0.3 ± 0.6	0.59, Mann-Whitney test
Standing cough stress test positive	57%	74%	0.06, χ^2 test
Urodynamic diagnosis			0.60, χ^2 test
Detrusor instability only	23%	23%	
Genuine stress incontinence only	53%	46%	
Mixed incontinence	23%	31%	
Maximum cystometric capacity (ml)	410.7 ± 159.1	415.1 ± 165.2	0.88, pooled-variable t test

Table IVA. Urodynamic diagnosis of detrusor instability

Detrusor instability before	*Detrusor instability*			
	After sham		*After stimulation*	
	Positive	*Negative*	*Positive*	*Negative*
Positive	23	5	14	18
Negative	1	28	2	25

Table IVB. Urodynamic diagnosis of genuine stress incontinence

Genuine stress incontinence before	*Genuine stress incontinence*			
	After sham		*After stimulation*	
	Positive	*Negative*	*Positive*	*Negative*
Positive	41	3	41	5
Negative	0	13	3	8

Sixty (49.5%) of the subjects had pure genuine stress incontinence, 28 (23.2%) had pure detrusor overactivity, and 33 (27.3%) had mixed incontinence. A total of 61 (50.4%) participants were randomized to receive stimulation with the electrically active device, whereas 60 (49.6%) were randomized to receive a sham device.

Subject compliance was acceptable with a mean compliance of 87% and 81% at 4 and 8 weeks of treatment, respectively.

There was no statistically significant difference between the sham and stimulation groups with respect to compliance. No clinically or statistically significant differences were found between the stimulation and sham groups with respect to any of the background variables in Table III. In addition, there were no statistically significant differences between the treatment groups with respect to any of the pretreatment quality-of-life scale variables.

All patients with urodynamic confirmation of genuine stress incontinence reported symptoms of stress urinary incontinence. Almost half of patients with pure genuine stress incontinence also reported symptoms of urge incontinence (n = 46). Sixty-three percent of patients with pure detrusor overactivity on urodynamic testing reported symptoms of stress urinary incontinence. This is consistent with many reports indicating that subjective symptoms and current methods for objective confirmation are imperfectly related. Excessive missing data made analysis of the urinary diaries impossible.

Objective outcomes. The treatment groups differed markedly in the posttreatment urodynamic diagnosis of detrusor overactivity (Table IVA). Fifty-four percent of participants (n = 33) in the stimulation group had detrusor overactivity. After treatment, this percentage dropped by half to 27% (n = 16). This decrease was highly statistically significant (p = 0.0004, McNemar's test). In contrast, 47% (n = 28) of the sham subjects had

Table V. Additional outcome variables

Outcome variable	*Sham*	*Electric stimulation*	*Significance (sham vs electric stimulation)*
6 wk 24 hr frequency (average)	9.5 ± 2.8	9.3 ± 6.8	0.049, Mann-Whitney test
6 wk No. of accidents/24 hr (average)	2.2 ± 2.7	2.4 ± 3.1	0.75, Mann-Whitney test
Adequate subjective improvement	17%	35%	0.027, χ^2 test
8 wk compliance (%)	83.7 ± 14.7	78.8 ± 20.5	0.25, Mann-Whitney test
Final urodynamic diagnosis of detrusor overactivity	41%	27%	0.22, McNemar's test

detrusor overactivity before treatment, with a statistically nonsignificant posttreatment drop to 41% (p = 0.22, McNemar's test). There was no statistically significant change in the rate of genuine stress incontinence for either treatment group (Table IVB).

There were no statistically significant differences between the stimulation and sham groups with respect to any of the outcome variables shown in Table V. In addition, there were no statistically significant differences between the treatment groups with respect to any of the quality-of-life scale variables during or after treatment. Interpretation of the urinary diaries was not possible because of large amounts of incomplete patient data.

Comment

The most striking finding in this study was that about half of patients with detrusor overactivity had an objective cure of this condition with transvaginal electrical stimulation. Cure of detrusor instability occurred equally in women with or without coexisting genuine stress incontinence.

The neuronal mechanism that causes detrusor inhibition in select individuals remains to be clarified. There is sufficient animal evidence to implicate reflex pathways involving the pudendal-to-hypogastric, as well as pudendal-to-pelvic, pathways.[7] Vodusek et al.[8] have demonstrated that it is not necessary to have a motor response to achieve bladder inhibition in humans. Moreover, it is likely that there is a neurophysiologic relationship between the necessary current strength and the reflex threshold.[8] Further studies are necessary to appropriately select patients for this form of therapy.

Other methods of stimulation for detrusor inhibition have been reported. Ishigooka et al.[9] reported the use of percutaneous implantable electrodes in 10 patients, with complete resolution in 2 patients and improvement in an additional 6 patients. This technique has a theoretical advantage of more efficient current delivery; however, the invasiveness must be weighed against the results, which are similar to those for external removable devices. This study used intermittent home stimulation. Other nonrandomized trials have reported efficacy with acute office-based stimulation.[10, 11] The best method for stimulation may vary for individual patients.

The best single outcome measure for urinary incontinence remains elusive. We attempted to use both subjective and objective outcome parameters in this study. It was not surprising to us that the subjective response was less than the objective response. Almost one third of our subjects had mixed incontinence; thus they might easily have had continued incontinence as a result of the persistence of stress incontinence, despite cure of detrusor instability.

Unfortunately, validated disorder-specific instruments for quality-of-life assessment were not available at the initiation of this study. The instrument that we used was inadequate, despite promising pilot data. Standardized measures have since become available and should be included in subsequent studies of this topic. As pointed out by Testa and Simonson,[12] quality-of-life effects should not be ignored simply because they are difficult to measure.

The previously standardized patient diary proved so burdensome to our study participants that there was a high rate of incomplete diaries. This low rate of diary completion may have been caused, in part, by the fact that our study participants were not compensated in any manner for their participation, because support was limited to provision of the active and sham electrical stimulators.

Several findings were unexpected. One site (Methodist) had an unusually high dropout rate. Nine of these patients dropped out before treatment. The Methodist site serves a broad geographic area, and travel inconvenience was frequently cited as a reason for dropping out.

In addition, there were erratic, transient technical problems with the electric stimulation device, which caused delays with the timely completion of the study in several sites. These problems appeared to be caused by a loose electrical connection within the motherboard. Initially, there was concern that the stimulation group had subjects who were not receiving any stimulation. All active units were checked manually to ensure that an electric stimulus was provided. Subjects with intermittent technical problems had previously felt the electrical stimulus, and all promptly reported changes in sensation during treatment.

The device studied in this investigation represents only one of many available devices for transvaginal electric stimulation. In addition, the electric settings we used were device dependent and relatively empiric. Whereas animal data suggest the appropriateness of these parameters, human studies have not yet been reported.[13, 14] More refined choices of these settings are pending individual studies of each parameter.

Despite the large number of variables examined in this study, we believe that it is likely that other variables may account for the varying efficacy in the stimulation group. Such variables may include aspects of the neuromuscular milieu that are only crudely assessed during the general urogynecologic physical examination. This idea is particularly enticing because of the known neural role of detrusor overactivity.

This study did not reproduce the findings of Sand et al.,[4] in which efficacy for genuine stress incontinence was reported. The differences may be explained by differences in method of stimulation, patient population, or selected outcome measures. Our study has insufficient statistical power to conclude a lack of efficacy for genuine stress incontinence.

Electric stimulation does appear to be objectively effective for the treatment of detrusor overactivity. It is well established that detrusor overactivity is a medical, not surgical, disorder, so that nonsurgical treatment is appropriate. Given the systemic side effects of current pharmacotherapy, transvaginal electric stimulation should be considered first-line therapy. However, significant refinement in this therapy may be possible with further study of the cystometric and neurophysiologic status of patients with detrusor overactivity. In particular, refinement of the mode and manner of electrical stimulation is likely.

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