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Efficacy of Functional Electrical Stimulation in Treating Genuine Stress Incontinence: A Randomized Clinical Trial

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Our objective was to determine the efficacy of functional electrical stimulation as a stand-alone therapy for female stress incontinence. The study was conducted as a prospective, double-blind, randomized controlled trial using subjective and objective outcome criteria. Patients enrolled in this study had stress incontinence consistent with International Continence Society criteria. Patients with significant pelvic prolapse or detrusor instability were excluded. Patients underwent twice-daily treatment sessions for a total of 3 months. Results were analyzed for confounding variables between the treatment and control groups. Statistical analysis was performed utilizing Fisher's exact test and the paired t-test. Of the 54 patients enrolled in this study, 44 completed the program. The dropout rate was similar for both the treatment and control groups. There was no statistically significant difference between the treatment and control groups with regard to age, gravity, parity, previous antiincontinence surgery, menopausal status, or previous hysterectomy. Objective success for the treatment group was 15% and for the control group, 12.5% (NS). The subjective success for the treatment group was 25% and for the control group, 29% (NS). There was no relationship demonstrated between age, parity, previous surgery, hysterectomy, or menopausal status and the successful treatment of genuine stress incontinence with functional electrical stimulation. In this patient population, functional electrical stimulation was no more effective at improving or eliminating the symptoms of genuine stress incontinence than was the daily retention of the control probe. *Neurourol. Urodynam. 16:543–551, 1997.*

Key words: functional electrical stimulation; genuine stress incontinence; physical therapy

INTRODUCTION

Urinary incontinence affects approximately 13 million Americans and costs an estimated $15 billion annually in the United States alone [Fantl et al., 1996]. Genuine

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stress incontinence results in an estimated 50,000 antiincontinence procedures performed annually. As we become aware of the epidemic proportions of the problem of female urinary incontinence and the cost and limitations of surgical intervention it becomes evident that we must seek effective nonsurgical management. Recent data confirm that antiincontinence procedures have a one-in-five rate of failure even in the hands of master surgeons [Trockman et al., 1995; Alcalay et al., 1995]. Functional electrical stimulation of the muscles of the pelvic floor was originally proposed in 1963 to address fecal and urinary incontinence [Caldwell, 1963]. Subsequent animal studies helped to define the mechanism by which functional electrical stimulation theoretically improved continence [Fall et al., 1977; Lindstrom et al., 1983; Ohlsson et al., 1986]. Since then, numerous clinical trials have reported on the efficacy of functional electrical stimulation in treating genuine stress incontinence, detrusor instability, and mixed incontinence [Eriksen and Eik-Nes, 1989; Eriksen et al., 1987; Fall et al., 1986]. The majority of these studies were performed without controls. In 1993, we began a prospective, randomized, double-blind, placebo-controlled trial to study the effectiveness of electrical stimulation in treating women with genuine stress incontinence.

MATERIALS AND METHODS

This study was conducted in a single medical center and funded by a grant from the Kaiser Research Foundation (grant 01-990-6571), with approval by and supervision of the institutional review board. The objective of the study was to determine the efficacy of functional electrical stimulation as a therapy for female genuine stress incontinence. The study was designed as a prospective, randomized, double-blind, placebo-controlled clinical trial. The study population consisted of women with genuine stress incontinence and no evidence of detrusor instability, as outlined below. Outcome measures included subjective assessment of improvement or cure by patients using a structured interview and questionnaire and objective assessment, including complete urodynamic investigation following completion of treatment.

All patients enrolled in the trial were initially seen and evaluated in the Department of Urogynecology (Southern California Permanente Medical Group, San Diego). Patients underwent an initial evaluation utilizing a voiding diary, questionnaire, structured interview, medical history, physical examination, and multichannel urodynamics. Physical examination included a general neurologic survey as well as focused neurologic examination of the lower extremities and pelvis, a pelvic examination including bimanual and speculum examination with grading of pelvic support defects, and a rectal examination. Hypermobility of the urethrovesical junction was assessed using a cotton-tip applicator placed in the urethra and maximum Valsalva effort and cough. Patients were offered enrollment in the study if they demonstrated genuine stress incontinence in the absence of detrusor instability and had failed an attempt or chose not to pursue pelvic floor rehabilitation utilizing pelvic floor muscle exercises. Inclusion criteria were defined as a diagnosis of genuine stress incontinence consistent with International Continence Society criteria, the ability to adequately retain the vaginal probe and to cooperate with the study protocol, and the ability to understand randomization and give informed consent. Exclusion criteria included pelvic organ prolapse of grade II or greater, detrusor instability, postvoid residual urine >100 cc, extra urethral incontinence, history of vaginal intraepithelial neoplasia,

evidence of vaginal or urinary tract infection, a fixed, immobile urethra, and urodynamic evidence consistent with intrinsic sphincteric deficiency. Grade II prolapse was defined as prolapse to the level of the vaginal intriotus. Urethral immobility was defined as excursion of a cotton tip applicator of <30° from the horizontal with maximum Valsalva and cough. Intrinsic sphincteric deficiency was defined as a leak point pressure of ≤60 cm or a maximum urethral closure pressure of ≤20 cm [McGuire et al., 1993; Sand et al., 1987].

Patients identified as eligible for enrollment in the urogynecology clinic were offered enrollment and consented using written materials and discussions with the principal investigator. Once consented and enrolled, patients were randomized into active vs. control groups. Randomization into the active vs. control arm of the study took place using opaque envelopes. Records of the randomization sequence were maintained by clerical staff without direct contact with the enrolled patients or study personnel. Patients were introduced to electrical stimulation in an office setting by a physical therapist who directed patients in the optimal use of the device per the manufacturer's guidelines and consistent with parameters established in previous studies. The principal investigator was not involved in initiation of therapy. Blinding was accomplished by having all patients use the same electrical stimulation device and probe and running the same program on the device. Patients randomized to the control group were issued vaginal probes in which the wiring from the unit to the probe was covertly discontinuous. All patients were informed that they may or may not appreciate sensation during stimulation sessions. Patients were separated from other patients participating in the study by staggering office visits. Patients were contacted biweekly thereafter by physical therapy and nursing personnel who remained blinded as to the patient's randomization sequence. Patients were also seen on an as-needed basis for complaints of pain, etc.

Stimulation took place in two 15-min treatment sessions per day over the course of 12 weeks, using a commercially available electrical stimulation unit (Hollister, Evanston, IL). The units were programmed to utilize a pulse-width of 2 msec, a work schedule of 2 sec followed by a rest schedule of 4 sec, a frequency of 50 Hz, and an adjustable power setting which ranged from 10–100 mA. Compliance was measured with an internal memory system within the stimulation unit which was downloaded to an office-based computer. At the completion of the 12-week trial, patients were reevaluated using voiding diaries, an incontinence questionnaire, and reexamination including multichannel urodynamic studies. The questionnaire administered after completion of the trial was identical to that administered prior to treatment, with the exception of several additional questions regarding the convenience, comfort, and effectiveness of the intervention, which were answered on a visual scale of 1–5 with 5 being the most desirable outcome. The questionnaire used has not undergone formal psychometric validation.

Patients were considered a subjective failure if they reported minimal or no improvement in symptoms after treatment (questionnaire scale 1 and 2). They were considered a subjective improvement if they reported moderate improvement in their symptoms (questionnaire scale 3 and 4). They were considered a subjective cure if they reported complete resolution of their symptoms of stress incontinence (questionnaire scale 5). Objective cure was defined as a negative stress test on repeat urodynamics with a full bladder. Likewise, objective failure was defined as a positive stress test on repeat studies.

The study was designed with the assumption that the control group of patients would have a spontaneous recovery rate of 10% and the group treated with electrical stimulation would have a response rate of 50%. Detection of this difference with a test that has a level of significance of 0.05, a power of 0.90, and 2 interim analyses would have required a maximum of 57 total subjects. The interim analyses were intended to provide statistical evidence for termination of the study in the event that there were no differences between the two arms in efficacy rates or if one arm were significantly superior to the other. Information regarding the patient's experience in the trial was coded on standardized forms, and the data were analyzed independently by the Department of Biostatistics, Southern California Permanente Medical Group, using the SAS statistical package (SAS Institute, Chapel Hill, NC). Fisher's exact test, 2 sample-paired t-tests, and the kappa coefficient were used where appropriate.

RESULTS

Sixty-seven women were offered participation in the study. Fifty-four women were enrolled in the study between June 1993 and January 1995. Forty-four of the subjects completed the trial and posttrial evaluation: 20 in the treatment group and 24 in the control group. The mean age of patients enrolled in the trial was 53.9 years (±10.3) and the average parity was 2.5 deliveries (±1.3). Thirty-one of the women were postmenopausal (72%) and 18 had undergone hysterectomy (42%). Ten patients had undergone previous antiincontinence procedures (23%). The median leak-point pressure was 90 cm of water (±21) and the average compliance with therapy was 82%. There was no statistically significant difference between the treatment and control groups with respect to potentially confounding variables (Table I). The majority of women were Caucasian (91%), with 2 women of African-American heritage and 2 women of Pacific-Islander heritage. Of those patients completing the trial and evaluation, we observed no statistically significant difference in the rate of subjective improvement, subjective cure, or objective cure between the treatment and control groups (Table II). Those who responded in either the treatment or control group were found to be similar to nonresponders, with no statistical difference between the groups with regard to age, parity, prior hysterectomy, prior antiincontinence surgery, prior pelvic muscle exercise, and menopausal status. A good concurrence between the objective and subjective measures was appreciated with a kappa coefficient of 0.32. Additionally, no difference was observed between treatment and control groups with respect to number of incontinence episodes, convenience and comfort of device use, post void residual, cystometry or leak point pressures (Table III). The dropout rates and dropout indications were similar in the two groups (Table IV). There was one death occurring in the treatment group that was unrelated to device use. Information on patients who discontinued participation in the trial was incomplete and not analyzed. No complications related to device use were observed, i.e., no vaginal bleeding, vaginal erosions, urinary tract infections, worsening of urinary incontinence, electrical accidents, or discomfort that persisted after device removal. The study was discontinued after interim analysis revealed that after enrollment of 54 patients, no difference was observed in the outcomes between the two groups.

DISCUSSION

In this study population, electrical stimulation of the pelvic floor was found to be no more effective in treating genuine stress incontinence than was the retention of

TABLE I. Comparison of Treatment and Control Groups

	Treatment	Control	*P*-value
Enrolled	26.0	28.0	
Dropout	6.0	4.0	>0.05
Age	54.1	53.6	>0.05
Parity	2.6	2.5	>0.05
Previous surgery[a]	4.0	6.0	>0.05
Hysterectomy	8.0	10.0	>0.05
Menopausal	11.0	20.0	>0.05
Prior PME[b]	18.0	16.0	>0.05

[a]Previous antiincontinence surgery.
[b]PME, pelvic muscle rehabilitation.

TABLE II. Comparison of Outcomes for Treatment and Control Groups Following 12 Weeks of Electrical Stimulation

	Treatment	Control	*P*-value[a]
Subjectively improved[b]	3 (15.0)	3 (12.5)	1.000
Subjectively cured[c]	2 (10.0)	4 (16.7)	0.785
Objectively cured[d]	3 (15.0)	3 (12.5)	1.000

[a]Fisher's exact test.
[b]Patients reporting moderate improvement (scale 3–4).
[c]Patients reporting resolution of stress symptoms (scale 5).
[d]Stress test negative.

TABLE III. Parameters for Control and Treatment Groups Before and Following 12 Weeks of Electrical Stimulation

	Control		Treatment	
	Pre	Post	Pre	Post
Incontinence episodes per 24 hr[a]	2.7 (1–12)	2.4 (0–11)	2.8 (1–9)	2.4 (0–9)
Convenience of device use[a,b]	NA	3.2 (1–5)	NA	3.4 (1–5)
Comfort of device use[a,b]	NA	4.1 (1–5)	NA	3.9 (1–5)
Valsalva leak-point pressure (cm H_20)[a]	84.0 (62–135)	80.0 (66–130)	79.0 (67–121)	86.0 (65–127)
Cystometrogram maximum (cm^3) volume[a]	442.0 (311–623)	465.0 (320–640)	421.0 (336–593)	470.0 (316—630)
Postvoid residual (cm^3)[a]	21.0 (4–41)	19.0 (4–36)	18.0 (3–39)	23.0 (5–35)

[a]No significant differences observed between pre- and posttreatment parameters or between treatment and control groups.
[b]From questionnaire scale 0–5, with 5 representing optimal outcome.
Numbers in parentheses = range.

the placebo probe for an equal length of time. Sixteen percent of the treated patients and 13% of the control patients showed objective cure (NS). Twenty-five percent of the treated group and 29% of the control group reported either subjective improvement or cure. This is consistent with some previous investigations, but contrasts with

TABLE IV. Indications for Discontinuance of Therapy

Indication	Treatment	Control	*P*-value
Discomfort	3	2	>0.05
Discouragement	2	2	>0.05
Death[a]	1	0	>0.05
Total	6	4	>0.05

[a]Unrelated to device use.

others [Leach and Bavendam, 1989; Bo and Maaum, 1994; Sand et al., 1995; Ericksen and Eik-Nes, 1989; Fall et al., 1986]. Differences in study design, patient populations, and outcome measured may explain many of these differences.

Many previous studies that reported good results using electrical stimulation to treat stress incontinence failed to include control groups in their study design [Ericksen et al., 1987; Ericksen and Eik-Nes, 1989; Fall et al., 1986]. This is particularly important when a treatment such as electrical stimulation is being evaluated because the potential effects of even the placebo intervention may extend beyond simple placebo effects. It is quite possible that retention of the vaginal probe alone may effect improvement of pelvic muscle function as a result of the feedback created by retaining the probe. Some investigators have had patients retain electrical stimulation probes for up to 12 hr per day [Ericksen et al., 1987]. It could be argued that the benefit realized in such a situation is the result of the probe acting much like a vaginal cone. Indeed, we use vaginal cones to successfully treat genuine stress incontinence, and the probe of an electrical stimulation unit retained for a similar length of time, particularly if the patients are sitting or standing, may be expected to have results similar to the use of vaginal cones [Wilson and Borland, 1990].

Many previous studies also included patients with both genuine stress incontinence and detrusor instability [Fall et al., 1986]. This is problematic, as electrical stimulation is also used and is capable of downregulating detrusor activity [Vodusek et al., 1986; Sundin et al., 1974]. Once the symptoms of such a patient improve, it is unclear whether the improvement is a result of decreased detrusor instability or decreased stress incontinence. Such confounding variables make interpretation of these mixed studies difficult. The current study sought to eliminate this potential confusion by limiting enrollment to women with genuine stress incontinence who reported little or no urgency and demonstrated no detrusor instability on cystometry.

Other investigators have addressed the question of the efficacy of electrical stimulation, using controls with different results. Sand et al. [1995] looked at a population of 52 women with genuine stress incontinence using a 2-to-1 randomization sequence, a placebo-controlled population, and predefined outcome criteria for improvement and cure. Patients were considered subjectively improved if the number of incontinence episodes per week was reduced by $\geq$50% and were considered subjectively cured if they reported no further episodes of urinary incontinence. Patients were considered objectively improved if they demonstrated a reduction in loss of urine of >50% on pad testing and were considered objectively cured if the pad tests demonstrated a loss of <1 g. Although they reported no statistically significant difference between the treated and control groups regarding either subjective or objective cure, they did detect an improvement in the study group regarding both subjective and objective improvement that was greater than that seen in the control group ($P <$

0.05). This may well reflect the use of a more sensitive instrument to measure outcome. The dropout rates in the treatment arm of the study were high when compared to the control arm (20% vs. 6%).

Attempting to blind patients in an intervention like electrical stimulation, which can be appreciated in its active form by the study participant, creates methodological difficulties. It must be assumed that a percentage of the patients in the active arm will become aware that they are receiving the intended treatment. However, this should bias results in favor of the active arm, which did not happen in this study. Additionally, as long as patients in the control arm remain isolated from the active arm, the placebo effect should not be compromised. In fact, several patients in the control arm complained of discomfort associated with the stimulation portion of the treatment cycle as indicated by a green light on the stimulation unit, despite receiving no actual stimulation. Compliance with treatment and dropout rates were similar in both arms of the study as well. This would not be expected if the blinding of the study had been compromised. Physicians performing follow-up urodynamics also remained blinded as to the patients' subjective impression of outcome and randomization sequence until completion of the patients' enrollment.

The current study is limited by its failure to use a disease-specific and validated quality-of-life instrument in assessing patients' progress. Unfortunately, such instruments were not available at the time that the study was designed and begun. Future studies will benefit from the use of currently available instruments [Schumacher et al., 1994; Wagner et al., 1996]. The population studied also contained a heterogeneous mix of women who had attempted to improve their incontinence symptoms through independent pelvic muscle exercise and women who did not wish to pursue such exercises. Although this reflects ''real practice'' in our institution, it may have biased the work by including women who had not improved with independent exercise and were thus less likely to improve with the enhancement of exercises that electrical stimulation might offer. Pad testing was not used to measure patients' incremental improvement. Although this information may have allowed us to objectify improvement beyond simple stress testing, we are unaware of a correlation between pad testing and a validated quality-of-life instrument. Voiding diaries were kept, but only for 24-hr periods pre- and posttreatment. Thus we lack statistically significant data regarding the change in incontinence episodes, and this also limited the study's ability to detect incremental changes in the patients' symptoms.

It is important that electrical stimulation as well as all other nonsurgical means of treating genuine stress incontinence continue to be evaluated in an objective manner. There may be technical modifications that foster more significant benefits than demonstrated in this study. For example, some investigators would recommend a longer stimulation period of 10 sec and a lower stimulation-to-relaxation ratio of 1/5 [Appell, 1987]. It may also be argued that electrical stimulation should not be expected to provide dramatic results in women with stress incontinence because there is evidence that electrical stimulation is of limited value in rehabilitating denervated muscle and there is substantial evidence that denervation of the pelvic muscles secondary to injuries imposed during vaginal delivery is in part responsible for stress incontinence [Scott et al., 1986; Gilpin et al., 1989; Smith et al., 1989]. Many believe that electrical stimulation will find its role in ''jump-starting'' the pelvic floor muscles in women otherwise unable to perform such exercises. This teaching role of

electrical stimulation has been used to facilitate biofeedback-enhanced pelvic floor muscle rehabilitation in patients with stress incontinence.

CONCLUSIONS

The current study demonstrated no efficacy in treating female stress incontinence with functional electrical stimulation. Future studies designed with appropriate control populations will further enhance our understanding of electrical stimulation and its possible role in the treatment of women with genuine stress incontinence.

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REFERENCES

Alcalay M, Ash M, Stanton SL (1995): Burch colposuspension: A 10–20 year follow-up. Br J Obstet Gynaecol 102:740–745.

Appell HJ, Cabric M (1987): The use of electrical stimulation for the strengthening of muscles in therapy and rehabilitation. Physikalische Therapie 8:8–17.

Bo K, Maaum M (1996): Does vaginal electrical stimulation (Conmax and Medicon MS-105) cause pelvic muscle contraction? Scand J Urol Nephrol Suppl 179:39–45.

Caldwell KPS (1963): The electrical control of sphincteric incontinence. Lancet 2:174–175.

Ericksen BC, Bergmann S, Mjolmorod OK (1987): The effect of anal electrical stimulation with the ''Incontan'' device in women with urinary incontinence. Br J Obstet Gynaecol 94:147–156.

Ericksen BC, Eik-Nes SH (1989): Long-term electrical stimulation of the pelvic floor: Primary therapy in female stress incontinence? Urol Int 44:90–95.

Fall M, Erlandson BE, Carlsson CA, et al. (1977): The effect of intravaginal electrical stimulation on the feline urethra and urinary bladder: Neuronal mechanisms. Scand J Urol Nephrol [Suppl] 44:19–30.

Fall M, Ahlstrom K, Carlsson CA, et al. (1986): Contelle: Pelvic floor stimulator for female stress-urge incontinence. Urology 17:282–287.

Fantl AA, Newman DK, Colling J (1996): Urinary incontinence in adults: Acute and chronic management. Clinical practice guidelines, number 2, 1996 update. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. Agency for Health Care Policy and Research. AHCPR publication number 96-0682. March 1996.

Gilpin SA, Gosling JA, Smith ARB (1989): The pathogenesis of genitourinary prolapse and stress incontinence of urine. A histological and histochemical study. Br J Obstet Gynaecol 96:15–23.

Leach GE, Bavendam TG (1989): Prospective evaluation of the Incontan transrectal stimulator in women with urinary incontinence. Neurourol Urodyn 8:231–325.

Lindstrom S, Fall M, Carlsson CA, et al. (1983): The neurophysiologic basis of bladder inhibition in response to intravaginal electrical stimulation. J Urol 129:405–410.

Mcguire EJ, Fitzpatrick CC, Wan J (1993): Clinical assessment of urethral sphincter function. J Urol 150:1452–1454.

Ohlsson E, Lindstrom S, Erlandson EE (1986): Effects of some different pulse parameters on bladder inhibition and urethral closure during intravaginal electrical stimulation: An experimental study in the cat. Med Biol Eng Comput 24:27–33.

Sand PK, Bowens LW, Panganiean R, et al. (1987): The low pressure urethra as a factor in failed retropubic urethropexy. Obstet Gynecol 69:399–402.

Sand PK, Richardson DA, Staskin DR, et al. (1995): Pelvic floor electrical stimulation in the treatment of genuine stress incontinence: A multicenter, placebo controlled trial. Am J Obstet Gynecol 173:72–79.

Scott OM, Vrbova G, Hyde SA, et al. (1986): Effects of electrical stimulation on normal and diseased

muscle. In Nix WA, Vbrova G (eds): ''Electrical Stimulation and Neuromuscular Disorders.'' New York: Springer-Verlag, pp 114–124.

Schumacher SA, Wyman JF, Ubersax JS, et al. (1994): Health-related quality of life measures for women with urinary incontinence: The Incontinence Impact Questionnaire and the Urogenital Distress Inventory. Quality Life Res 3:291–306.

Smith ARB, Hosker GL, Warrell DW (1989): The role of pudendal nerve damage in the aetiology of genuine stress incontinence in women. Br J Obstet Gynaecol 96:29–32.

Sundin T, Carlsson CA, Kock NG (1974): Detrusor inhibition reduced from mechanical stimulation of the anal region and from electrical stimulation of the pudendal nerve afferents. Invest Urol 11:374–378.

Trockman BA, Leach GE, Hamilton J, et al. (1995): Modified Pereyra bladder neck suspension: 10 year mean followup using outcomes analysis in 125 patients. J Urol 154:1841–1847.

Vodusek DE, Light JK, Libby JM (1986): Detrusor inhibition induced by stimulation of pudendal nerve afferents. Neurourol Urodyn 5:381–389.

Wagner TH, Patrick DL, Bavendam ML, et al. (1996): Quality of life of persons with urinary incontinence: Development of a new measure. Urology 47:67–72.

Wilson PD, Borland M (1990): Vaginal cones for the treatment of genuine stress incontinence. Aust N Z J Obstet Gynaecol 30:157–160.