UPDATE ON EXTRACORPOREAL MAGNETIC INNERVATION (ExMI) THERAPY FOR STRESS URINARY INCONTINENCE

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ABSTRACT

Pulsed magnetic technology has been developed for pelvic floor muscle strengthening for the treatment of urinary incontinence. This report includes an update of the prospective multicenter study of extracorporeal magnetic innervation (ExMI) therapy for stress incontinence and a discussion of the possible mechanisms of action. Issues of patient selection for ExMI therapy will also be discussed. One hundred and eleven women with demonstrable stress urinary incontinence were studied. The mean age was 55 ± 13 years, and the mean duration of symptoms was 11 years. Ninety-seven completed ExMI therapy and analysis. Evaluation before treatment included bladder diaries, dynamic pad weight test, urodynamics, and a quality-of-life survey. For treatment the patients were seated fully clothed in a Neocontrol chair with a magnetic field therapy head in the seat. Treatment sessions were for 20 minutes, twice a week, for 6 weeks. After ExMI therapy, all of the measures were repeated at 8 weeks, including the dynamic pad weight testing and quality-of-life survey. At 6 months, further data were added, including repeat bladder diary, pad use, and quality-of-life survey. Forty-seven women completed 6 months of follow-up; of the 47, 13 patients were completely dry (28%) and 25 used no pad or less than 1 pad per day (53%). Pad use was reduced in 33 patients (70%). The median number of pads was reduced from 2.16 to 1 per day (Wilcoxon signed rank test, $P < 0.005$). The frequency of leak episodes was reduced from 3.0 to 1.7 at 6 months (Wilcoxon signed rank test, $P = 0.004$). Detrusor instability was demonstrated in 10 before and 6 after ExMI ($P < 0.05$). ExMI offers an alternative approach for the treatment of urinary incontinence. ExMI therapy is effective for both stress and urge incontinence. The best results are achieved in those patients who use no more than 3 pads a day and have had no prior continence surgery. UROLOGY **56** (Suppl 6A): 82–86, 2000. © 2000, Elsevier Science Inc.

Pulsed magnetic technology has been developed for pelvic floor therapy and the treatment of urinary incontinence. This is a novel application of a classic principle of physics, that a changing magnetic field will induce a flow of electrons within the field. Faraday's law of magnetic induction states that current will flow in a conducting medium in response to a changing magnetic field. Radiology has harnessed this principle to enhance the resolution of modern diagnostic imaging with magnetic resonance imaging (MRI) technology. Extracorporeal magnetic innervation (ExMI) uses a similar approach to induce controlled depolarization of adjacent nerves and contraction of muscles.

The physiologic stimulus of the pulsed magnetic field depends on some special design features that allow for a highly focused field and a very steep gradient of change at the advancing edge of the field. These characteristics produce a rapidly pulsing magnetic field that is readily adjustable in frequency and strength. The magnetic field will pass without significant attenuation through air, skin, fat, and even bone. For clinical effects, there is no advantage to be gained from removing the external clothing. The strength of the induced electric field at maximum output is 140 V/cm at the surface of the therapy head (pulse width 266 μsec), and this decreases exponentially with distance from the core. At 4 inches (10.2 cm) above the core, the field measures 22 V/cm. The magnitude of the field in the target tissue is approximately 80 V/cm. As the magnetic field pulses, the flux induces small eddy currents to flow in the tissues. These currents will

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FIGURE 1. *NeoControl pelvic floor therapy system. For treatment the patient is seated on a NeoControl chair.*

induce depolarization of nerve axons, and there will be a propagating nerve impulse that will travel both in a proximal and distal direction. If it is a terminal motor nerve axon, the propagating impulse will travel to the motor end plates and cause the obligatory release of acetylcholine, and there will be depolarization of the corresponding muscle fibers and contraction of those fibers. As the magnetic flux is regulated, the rate of contraction of the muscle fibers can be modulated within the usual physiologic ranges. It is possible to drive the rate of muscle fiber contraction to the maximum physiologic rate, on the order of 20 Hz.

The first clinical application of ExMI technology was for the treatment of urinary incontinence.[1] For pelvic floor therapy, the magnetic field generator (therapy head) is contained within the seat of the Neocontrol system (Neotonus, Inc., Marietta, Ga). It is situated in the middle of the seat and is controlled by an external power unit (Fig. 1). The output of the power unit consists of pulses of current, and the amplitude can be adjusted by the clinician. It is the amplitude that determines the volume of the field and thus whether it is strong enough to induce a nerve impulse.

METHODS

A total of 111 women with demonstrable stress urinary incontinence were included in a multicenter prospective study. All were ambulatory and neurologically normal. All subjects were using pads for protection. The mean age was 55 ± 13 years, and the mean duration of symptoms was 11 years (range 2 to 40). A total of 14 subjects failed to attend all treatments because of scheduling conflicts or travel problems, and they were excluded from the analysis. In all, 97 completed ExMI therapy and analysis; 3 bladder diaries were incomplete. Evaluation before treatment included two 3-day bladder diaries on successive weeks, a dynamic pad weight test, urodynamics, and a validated quality-of-life survey.[2]

For treatment, the patients were seated fully clothed in a Neocontrol chair. The adjustable parameters include the amplitude (25% to 100%), "on" interval (in seconds) and "off" interval (in seconds), and the frequency of the pulsed magnetic field (1 to 50 Hz).

Treatment sessions were for 20 minutes, twice a week, for 6 weeks. The frequency of the pulsed magnetic field was 5 Hz, intermittently for 10 minutes, followed by a rest period of 1 to 5 minutes and a second treatment at 50 Hz intermittently for 10 minutes. The treatment intervals were intermittent (5 seconds on and 5 seconds off) to avoid muscle fatigue. The patient was able to move about if she desired to during the rest period. The interval measures included bladder diaries and pad use. After ExMI, all of the measures were repeated at 8 weeks, including the 3-day bladder diary, dynamic pad weight testing, urodynamics, and the validated quality-of-life survey. At 6 months, further data were added, including repeat 3-day bladder diary, pad use, and the quality-of-life survey.

RESULTS

We have previously published the first results of a prospective multicenter study of ExMI for stress incontinence.[1] These early results were encouraging but limited by the lack of a placebo group and the short interval of follow-up. Of the 50 patients who had been observed for more than 3 months, 17 (34%) were dry, 16 (32%) were using not more than 1 pad per day, and 17 (34%) were using more than 1 pad per day. Pad use was reduced from 2.5 to 1.3 ($P = 0.001$), and the number of leak episodes was reduced from 3.3 to 1.7 ($P = 0.001$).

The interval of follow-up has been extended, and there are data now for 47 patients who have completed more than 6 months of follow-up. At 6 months, 13 patients were completely dry (28%), and 25 were using no pad or less than 1 pad per day (53%). Pad use was reduced in 33 patients (70%), and the median number of pads used per day was reduced from 2.2 to 1 (Fig. 2). This difference was significant on nonparametric analysis, mean rank for pad use at 6 months (Wilcoxon signed rank test, $P < 0.005$). The number of episodes of leakage was reduced. The ranges were wide (0.3 to 9.6 before and 0 to 11 leaks per day after ExMI), but the median value for leak episodes was reduced from 3.0 to 1.7 at 6 months (Wilcoxon signed rank test, $P = 0.004$). Seventeen patients who failed to reach maximal improvement with 6 weeks of ExMI therapy were entered in a further study with an extended interval of treatment, and a smaller number of patients requested further treatments. The data were analyzed by Sand *et al.*[3] to look for factors that may influence the outcome of ExMI at 2 weeks (n = 76) and at 6 months (n = 58) after therapy.

The changes in outcomes were evaluated using *t*

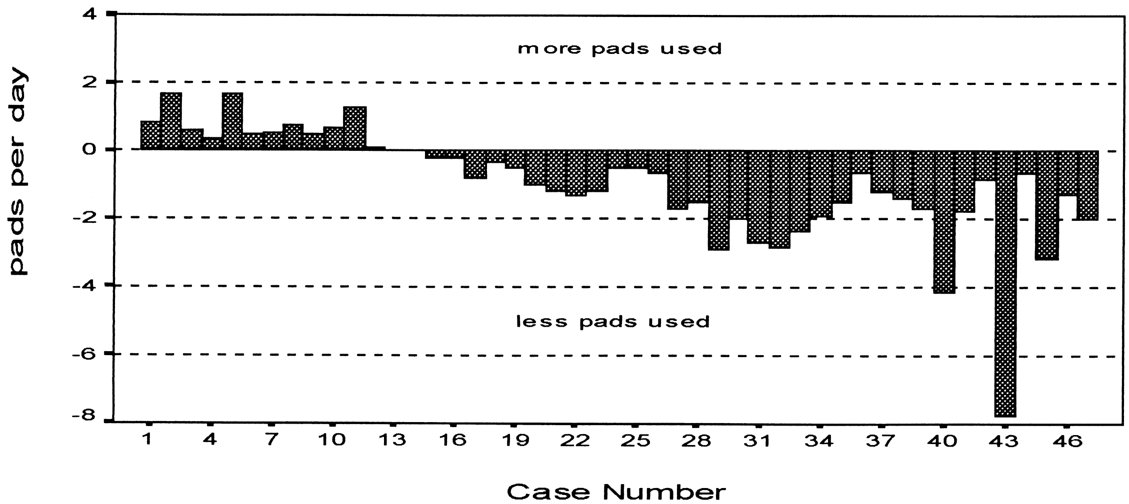

FIGURE 2. *Difference in pad use measured before and at 6 months after extracorporeal magnetic innervation (ExMI) therapy.*

tests and 1-way analysis of variance. Using multivariant analysis, Sand *et al.*[3] identified 3 factors that may be associated with a less favorable outcome. These factors include a history of failed surgery for incontinence, hysterectomy, and a duration of symptoms greater than 10 years. If these factors do not exist (n = 16), 69% are more than 50% improved and 44% are dry at 2 weeks. At 6 months with none of these factors (n = 14), 57% are more than 50% improved ($P = 0.005$) and 43% are dry. If there is a history of prior continence surgery and hysterectomy, 53% were improved after 2 weeks and 32% were dry, but at 6 months 40% were improved by more than 50% compared with baseline and only 18% were dry.[3]

The analysis of the validated quality-of-life measures (I-QOL) was studied by Bavendam (personal communication). I-QOL surveys were complete for 104 subjects. For the total group the mean score at baseline was 63, and this increased to 81 after ExMI therapy ($P = 0.0001$). Of those subjects who had a low score at baseline (all scores less than 66; n = 50), the mean score for this group was 47, and this increased to 70 after ExMI therapy ($P = 0.0001$). Further analysis of the I-QOL data and the correlation with bladder chart data and pad use will be presented later.

In a second group of female subjects, the impact on lower urinary tract symptoms (LUTS) was studied. Fifty-four patients reported an increased urinary frequency of 8 or more voids per day on the self-reported questionnaires before ExMI. After 6 weeks of treatment, 35 (65%) reported a decrease in urinary frequency ($P = 0.005$). Frequency was unchanged in 10 (18%) and increased in 9 (17%). Patients are very willing to accept this type of therapy. No adverse events were reported, and no subjects dropped out of the study because of side effects.

COMMENT

The lack of a control group has been seriously criticized. In the first report, the follow-up was only 3 months, and there must be concern about the magnitude of a placebo response. It would seem unlikely that the measurable sustained benefits at 6 months could be attributed to a placebo effect, but it is important to repeat this work and to include a blinded cross-over design with sham treatment. A sham device has been developed, and further studies that include a sham treatment group are in progress.

Yamanishi *et al.*[4] examined the effects of magnetic stimulation on urethral closure in healthy volunteers and published their findings. These independent investigators used a magnetic field generator device of a different design, but the principle is the same. During pelvic floor stimulation, they were able to demonstrate and record significant increases in maximum urethral closure pressures. A sham group was included in their study, and no urethral pressure change was noted in the control subjects. These authors concluded, "magnetic stimulation safely and significantly increased maximum intra-urethral pressure during stimulation."[4] This work does help to confirm 1 of the physiologic effects, but it does not offer direct evidence about the mechanism of action of ExMI in the treatment of incontinence.

Possible Mechanisms of Action of ExMI

Nerve tissue is particularly sensitive to the effects of eddy currents induced by the pulsed magnetic field. The key to the efficacy of ExMI is the depolarization of nerve fibers and the effects that the nerve impulses induce in the peripheral and central regions of the nervous system. The induced depolarization will pass distally to motor end plates and muscle fibers, but depolarization will also occur in sensory afferent fibers and autonomic nerves that may regulate local blood flow and other factors. The central actions are less clear, but for anyone who has experienced the sensations of ExMI therapy there can be no doubt that there are volleys of incoming sensory stimulation that travel the length of the central nervous system. One of the obvious clinical effects of ExMI is to change the activity of muscle groups in the pelvic floor. Repeated activation of the terminal motor nerve fibers and the motor end plates will tend to build muscle strength and endurance. It is also thought that ExMI might change the pattern and rate of firing of the motor nerve fibers responsible for the resting tone of the pelvic floor and sphincter muscles.

The pelvic floor muscles are broadly similar to other muscles—a composite of a number of similar anatomic and functional elements. Each element is called a motor unit and consists of a single motor neuron, its axon with motor end plates, and the respective muscle fibers that are activated by that nerve. The activity of the motor units is not static; it is dynamic and changing. The changing patterns of activity are reflected by the sounds of electromyography (EMG). The sounds of the urethral sphincter EMG range from complete silence during the volitional act of voiding, through quiet sounds at rest with an empty bladder, to louder sounds with bladder filling (recruitment), and finally loud crescendos of activity with coughing or straining.

The activity of each motor unit is all or nothing. Each motor unit has only 2 states, "on" or "off," and the overall muscle activity at any moment is the sum of all the motor units in the muscle. A common form of disordered firing pattern in skeletal muscle occurs when groups of motor units act together instead of acting independently. This is called coupling. We might think of this as notes on a piano keyboard that stick together instead of moving independently. It is not difficult to imagine how coupling might drive the system away from the normal versatile pattern toward synchrony (all units working together). More work is needed to explore these mechanisms. ExMI therapy may have a part to play in unlocking the coupled elements and helping to restore a more versatile range of sphincter muscle activity.

In addition to the physiologic patterns of neuromuscular activity, there are also pathologic patterns. In certain neurogenic disorders, ephaptic transmission has been demonstrated in skeletal muscle, and these changes may also occur in the striated muscle of the urethral sphincter. Ephaptic transmission is the depolarization of 1 muscle fiber by the electrical activity in an adjacent muscle fiber (muscle to muscle stimulation, rather than synaptic nerve to muscle stimulation). This pattern may play a role in involuntary muscle activity creating symptoms of cramps and muscle pain. These factors might also have a role in voiding dysfunction and episodes of urinary retention.

As we begin to view the pelvic floor as a population of motor units with firing patterns, it is possible to explain why it might be that a single episode of cystitis could provoke symptoms that persist even after the urinary infection has resolved. If cystitis might upregulate the firing patterns and produce sensations of urgency and frequency, it would seem possible that these changes might persist in some individuals, and perpetuate and sustain LUTS, even long after resolution of the infection episode that triggered the onset of symptoms.

In clinical practice, neuromuscular structures vary widely from 1 patient to another with a corresponding range of functions. The success of treatments varies according to the severity of the muscle weakness. Mild weakness can be improved by appropriate pelvic muscle exercises. Moderate weakness can be strengthened by exercise and biofeedback or by the use of electrical probes for stimulation.[5,6] ExMI offers a noninvasive alternative to induce contractions and improve muscle strength. Severely deficient muscles are characterized by atrophy and nerve and muscle cell death. It should be expected that for atrophic muscles, attempts to strengthen with exercises or stimulation might be less likely to succeed.

The treatment interval of 6 weeks was empirical. In practice, ExMI treatments may be continued for 8 or 10 weeks. Data will be available later to describe the effects of a longer treatment interval for those subjects who felt that they had not reached their maximal improvement and who elected to have further ExMI treatments. As we move to apply this technology in clinical practice, we should expect to add simple conservative strategies, such as fluid management, timed or prompted voiding, pelvic floor exercises, diet, and bowel management. There are opportunities to add value by including patient-directed education during ExMI therapy. This can be done using video, audio, and written materials to complement the ExMI therapy. We are confident that these efforts to educate the patient and to encourage successful management strategies and guarding techniques will serve to promote optimal outcomes and achieve durable benefits.

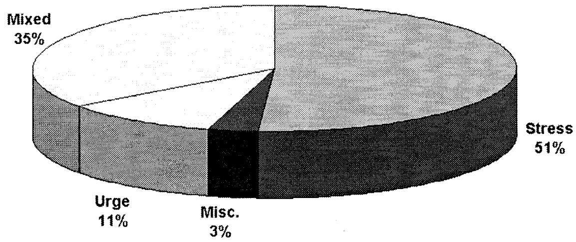

FIGURE 3. *NeoControl diagnosis mix by type of incontinence (January to October 1999). A total of 1000 patients were treated in clinical practice. This chart illustrates the principle indication for treatment: stress urinary incontinence in 51%, mixed incontinence in 35%, and urge in 11%. Miscellaneous indications include fecal incontinence and pelvic pain problems.*[7]

Current Clinical Utilization

In the first 12 months since US Food and Drug Administration clearance of ExMI, more than 1000 patients have been treated in the routine clinical setting (Fig. 3). The primary indication for treatment has been urinary incontinence. The type of incontinence was reported to be stress in 51%, mixed incontinence in 35%, and urge in 11%. An additional 3% of patients were treated for other problems that included fecal incontinence and pelvic pain. ExMI therapy offers a new approach for pelvic floor muscle strengthening, and the first benefits have been seen in the treatment of stress and urge incontinence. As physicians come to learn more about the importance of pelvic floor muscle dysfunction as a cause of the LUTS of urinary frequency, urgency, and nocturia, the clinical role for ExMI therapy will grow.

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