A novel approach to premature ejaculation: extracorporeal functional magnetic stimulation

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Introduction: *Premature ejaculation (PE) is a common sexual dysfunction. Treatment ranges from behavior modification to systemic and topical pharmacological treatments. Results to date have been generally inconsistent and of limited effectiveness. New avenues of therapy are needed.*

Aim: *To investigate the effect of extracorporeal functional magnetic stimulation (FMS) as a noninvasive treatment for men with PE.*

Methods: *The NeoControl System for FMS was used in the study. Baseline assessment included: history and physical, medications, hormonal assessment and intravaginal ejaculatory latency time (IVELT) by stopwatch determination. Treatment involved a first phase of five biweekly sessions (primary outcome). Men who reported an improvement in IVELT and desired to continue were given a second identical course (secondary outcome). Outcome measures included: IVELT and a global assessment questionnaire (GAQ). The responses incorporated both the patient's perception of response together with the more objective IVELT timing and were rated as: 1. Worse: no improvement in GAQ or mean IVELT for the total number of attempts; 2. Unchanged: improvement in IVELT but the patient reported no improvement; 3. Slightly improved: increase in IVELT < 100% and a reported mild improvement and 4. Better: IVELT increase of ≥ 100% with GAQ indicating "moderate" to "marked" improvement.*

Main outcome measures: *Two primary outcome measures were considered in both treatment phases, the IVELT and the GAQ.*

Results: *Fourteen men were treated. Their mean age was 43.7 years. Fifty-seven percent reported primary PE and 63% were circumcised. Hormone levels were normal in all. Baseline IVELT for the group was 60.6 seconds. All patients completed phase I. Of these, 50% reported no change in the GAQ although they recorded an increase in IVELT; 29% were categorized as slightly better and 14% as better. Eight men entered phase II. Of these, 3 (37.5%) were unchanged; 2 (25%) were slightly better and 3 (37.5%) were classified as better. The response in these last three has persisted for over 6 months post treatment. Both phases of the study showed a trend towards IVELT improvement, more evident at the end of phase II. However the differences did not reach statistical significance on either phase. Side effects were mild and non-treatment related.*

Discussion: *The use of FMS is claimed to alter the spinal centers without altering cerebral neurotransmitters. Although there were some remarkable responses, our results, are not better than the purported responses to behavioral or pharmacological methodologies. There was a clear trend in IVELT improvement; however, this didn't translate into an equivalent subjective estimation by most of the subjects. This outcome dissonance might be diminished by longer/more intense regimens of treatment. The pilot nature of the study does not permit to draw solid conclusions but stimulate the search for a new therapeutic option in PE.*

Key Words: premature ejaculation, electromagnetic nerve stimulation

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Introduction

The degree of emotional strain resulting from premature ejaculation (PE) is significant and affects the couple, as a unit, in variable degrees. When one or both partners seek professional help their decision should be seen as an indicator of substantial dissatisfaction and stress with their sexual life. Despite the large prevalence of PE, estimated to be as high as 30% of the adult population,[1,2] it remains incompletely understood and consequently, its treatment is diverse and frequently

nonspecific.[3] Thus, psychoanalytic therapies, are, by now largely abandoned; behavioral approaches are recognized for their limited and temporary success but led the way to pharmacological treatment, initially with tricyclic antidepressants and, later on with serotonin reuptake inhibitors (SSRIs).[4] Interest in new delivery forms of topical anesthetics has, recently rekindled[5] but their superiority over systemic pharmacotherapy remains unproven. A recent review failed to find conceptually new approaches that are needed for the treatment of PE.[6]

The current neurobiological explanation for PE advances the concept that serotonin and its receptors are the primary control of the ejaculatory reflex. It further postulates that serotonin mediated neurotransmission and activation of 5-HT_{1A} receptors accelerates ejaculation. These views have been documented in animal models and are offered as the rationale for the response to SSRIs in humans.[7] The efficacy and safety of SSRIs, however, leaves much room for improvement. Noninvasive magnetic stimulation of the central and peripheral nervous system was introduced 20 years ago and found to induce selectively higher electrical peripheral nerve depolarization.[8] Depolarization of motor nerves results in propagating impulses leading to muscle contractions. For this reason the technique has found its more obvious application in the treatment of urinary incontinence. More recently, Paick et al,[9] suggested that depolarization can also be induced in sensory afferent and autonomic nerves and reported encouraging results in patients with chronic pain syndrome. Based on these reports, we explored this therapeutic option in men with PE.

Materials and methods

Men with a diagnosis of primary or secondary PE and a stable heterosexual relationship were enrolled in a pilot study to determine whether the induction of electromagnetic fields in the pelvis would have an effect on their problem with PE. Inclusion and exclusion criteria are listed in Table 1. The baseline assessment included history and physical examination, assessment of medications, International Index of Erectile Function (IIEF) questionnaire to rule out erectile dysfunction, a hormonal evaluation consisting of gonadal steroids and thyroid stimulating hormone (TSH) and the intravaginal ejaculatory latency time (IVELT) by stopwatch determination. The treatment regimen comprised a first phase of five biweekly sessions which produced the primary outcome. Patients who reported an improvement in IVELT, did not show deterioration in symptoms and desired to continue, were administered a second identical course of treatment, phase II.

TABLE 1. **Inclusion and exclusion criteria**

Inclusion criteria
Legal age to sign consent
History of PE (couple distress because ejaculation earlier than desired and < 3min)
Exclusion criteria
Presence of a urinary tract infection
History of any genito-urinary cancer
History of cardiac arrythmias
Presence of pacemaker/ defibrillator
History of inflammatory bowel disease
History of pelvic surgery within 1 year
Presence of metallic implants
Presence of insulin pump
External monitor of any type
History of erectile dysfunction
Any treatment for PE within 8 weeks

Outcome measures included the mean IVELT recorded with stopwatch by the patient's partner after every attempt at sexual intercourse and a seven point Global Assessment Question (GAQ) where the patients were asked to rate their improvement as markedly worse, moderately worse, slightly worse, no change, slightly improved, moderately improved and markedly improved. The responses were then further grouped as: 1. *Worse*: no improvement in GAQ and/or in the mean IVELT for the total number of attempts; 2. *Unchanged*: if there was a recorded improvement in IVELT but the patient reported no subjective improvement; 3. *Slightly improved*: included those in whom there was an increase in IVELT of < 100% and the patients reported a mild improvement and 4. *Better:* comprising those with an IVELT increase of more than 100% and a GAQ indicating moderate to mild improvement. The study was approved by the University's Ethics Review Board.

The NeoControl System (Marietta, Georgia, USA) for extracorporeal electromagnetic nerve stimulation was used throughout the study. The system is comprised of a magnetic pulse generator and a treatment chair that houses the treatment head that produces the magnetic fields. The machine can generate a continuous current at a maximum frequency of 50 Hz with a stimulating pulse width of 720 microseconds and a maximum output at the 100% setting of more than 250 J for over 20 minutes.[10] For this study the patient treatment sessions were preprogrammed for 10 minutes at a frequency of 10 Hz, followed by a 2 minute rest period, and then 10 minutes at a frequency of 50 Hz (10 or

20 treatments). The power intensity was adjusted to the maximum tolerated setting (first indication of discomfort) at each session. With a single exception, all patients tolerated well the maximum power intensity. A complete description of the basic procedure has been published previously.[11] Briefly, when the patient sits in the Neo-control chair, the perineum is centered in the middle of the seat, thus placing the perineal muscles and nerves on the primary axis of the magnetic field. The course of treatment is specifically preprogrammed for each individual patient for the duration and the stimulating pulse output of the sessions.

The number of subjects is adequate for a pilot study and allows descriptive statistics. The Mann-Whitney Rank Sum test was used to compare mean IVELT before and after in the whole population and for the initial responders who participated in phase II.

Results

Fourteen men signed the informed consent and received at least one treatment. Their ages ranged from 19 to 68 (mean: 43.7) years. Primary PE was reported by 57% and 64% had been circumcised. All had satisfactory erectile function and none had abnormalities of either gonadal steroids, TSH or PSA (data not shown).

The IVELT for the group range between 2 and 134 seconds with a mean of 60.6 seconds, Table 2. All 14 patients completed 10 treatments (two sessions weekly for 5 weeks) fulfilling phase I of the study. Of the evaluable patients, 7/14 (50%) were considered to be unchanged, 4/14 (29%) were assessed as slightly better, and 2/14 (14%) were better. Although there was an increase in IVELT following the first course of therapy, the difference in median values did not reach significance (p = 0.190). The remaining patient rated his PE as worse and was therefore not eligible for phase II. Primary outcomes of GAQ and change in IVELT are shown in the Table 1. Eight men participated in the phase II of the study. Of these, 3 (37.5%) remained unchanged; 2 (25%) were considered slightly better and 3 (37.5%) were classified as better. Though the patient numbers are small, the IVELT response does show a trend to improvement over time, see Table 1; but the difference from the beginning and the completion of phase II, again, was not significant (p = 0.182), Figure 1. The response in the latter three men has persisted during the period of follow up ranging from 8 to 14 months (mean: 10 m). There were no significant adverse effects reported during or after treatment, see Table 3. All tolerated the 100% output with one exception that could not go above 85%.

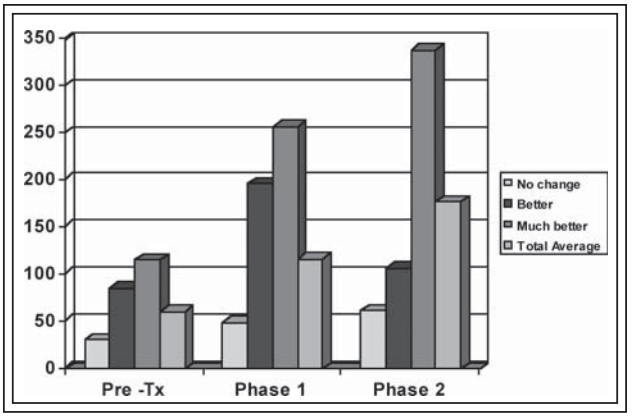

Figure 1. Changes in IVELT from pretreatment to completion of phase II in the eight patients who noticed benefit after phase I and wished to continue into the second phase. There is a trend to increase in IVELT from baseline to end of phase I and a further increase at the end of phase II. The average improvement in IVELT is shown in the last column for each phase. The GAQ (no change, better and much better –see text) is illustrated on completion of phases I and II.

Discussion

The combined use of counseling/psychotherapy together with the "stop-start" and squeeze techniques have been used since the middle of the 20th century with variable and sometimes contradictory results. A consensus exists, however that although these techniques may result in

TABLE 2. **IVELT**

GAQ ratings	**Phase I IVELT GAQ n = 14**	**Baseline IVELT sec (range)**	**Phase I IVELT sec (range)**
Slightly worse	1 (7%)	15	15
Unchanged	7 (50%)	49 (2-136)	76 (1-180)
Slightly better	4 (29%)	62 (31-134)	88 (48-143)
Better	2 (14%)	122 (116-129)	370 (257-482)

TABLE 3. **Adverse effects**

Side effects	
Cold symptoms	1
Improved bladder control	1
Urinary incontinence	1
Groin pain/discomfort	2
Forearm/shoulder pain	1
Increased erection strength and ejaculation force	1
Hangnail infection	1

adequate initial responses, the benefits are not long lasting.[12] The introduction of psychopharmacological approaches offered new possibilities. Their promises to date remain largely unfulfilled. Drawbacks of these techniques include unsatisfactory response rate, cost and time considerations, as well as potential side effects, including serious ones such as somnolence, dizziness, tremors, diarrhea and the unconfirmed concerns about "suicidality".[6] In addition, they are believed to be more effective with daily rather and "as needed" use,[13] which would further diminish its acceptance by the patients. The use of topical anesthetics is generating renewed interest and new delivery forms are currently under evaluation. Their major advantage is the absence of side effects frequently occurring with psychotropic drugs. Their position among the treatment options for PE remains to be firmly established.[5]

It is evident that the field of ejaculatory disorders is still very young, most therapies have not truly passed the test of time or the rigors of proper trials or are simply used in an "off-label" manner as result of serendipitous observations. This study does not pretend to be above any of them. The scientific basis for the use of electromagnetic fields in cases of PE are tenuous but, in our view, warranted because of the scarcity of specific therapeutic options focused on the etiology of the condition.

The theoretical base for the use of FMS originates from its ability to induce peripheral nerve depolarization affecting, primarily, motor fibers but also the sensory afferent and autonomic nerves.[9] Accepting that ejaculation is a sacro spinal reflex mediated by the pudendal nerve,[14] would lead to the possibility that the electromagnetic field create by FMS would translate in neuromodulation and, possibly an alteration in the characteristics of the sacro spinal reflex.[15] The magnetic stimulation is postulated to work in a manner similar to electrical stimulation but circumventing the discomfort/pain that occurs at the point of application of an electric functional stimulus. FMS has been reported to be efficacious in female urinary incontinence.[16]

The results illustrated in Table 2 suggest that men with the most severe ejaculatory dysfunction experienced the least response while the ones with longer IVELT values recorded the better subjective (GAQ) and objective (IVELT) responses. Whether a more intense or longer treatment is indicated for the worst cases cannot be determined by our results but remains an intriguing possibility worth exploring.

The efficacy of the various modalities to diagnose and treat PE is difficult to assess and there is a dismal lack of uniformity in the reporting. For starters, the AUA guideline is remarkably lax and vague in defining the condition as an "ejaculation that occurs sooner than desired…".[17] This chronological imprecision continues to be a source of difficulties to investigators since the definition of PE IVELT ranges from < 1 minute to up to 3 minutes. Most commonly, the patient's self reported distress, and interpersonal dissatisfaction are accepted, although the diagnosis becomes questionable if the IVELT is > 2 minutes. Partner's idiosyncrasies are usually ignored despite their obvious importance in the diagnosis and significance of therapeutic response. In most studies IVELT is considered the primary outcome measure and the efficacy of any given treatment is measured on the basis of the prolongation of IVELT as absolute change from baseline. IVELT is determined by stopwatch most often operated by the partner but occasionally by the patient who might overestimate it by a few seconds.[18] It is our view that an excessive reliance in the numeric mean of the IVELT by the stopwatch technique, although scientifically desirable, ignores the subjective but fundamental intimate emotional expectations of the couple that is so important for a fulfilling sexual experience. For PE studies, it appears to us that a more appropriate and realistic approach would give equal weight to IVELT numerical values and the couple's satisfaction report in the assessment of outcomes.

The results in this study are comparable to other series in which IVELT was determined prior to treatment and was < 1 minute. Thus Waldinger et al in control trials using paroxetine alone[19] or this and other SSRIs[20] and geometric mean latency reported increases from 17.1 sec. at baseline to 107.9 sec. at week 12 in one paroxetine study, and from 13 sec to 300 sec at 8 weeks in another. Their results for sertraline were 13.9 sec at baseline and 50.3 sec at week 6. Results from Waldinger's group have been consistent; the same cannot be said of the literature

on the topic in general. A comprehensive perspective of the discrepancies on reporting the type of study, number of patients, assessment of compliance and, above all the cacophony of outcome methodologies has been nicely summarized by Sharlip.[21]

FMS is essentially free of adverse effects although it requires investment of time, 10 sessions of 20 minutes each, at the very least. The cost for the cards to operate the equipment is approximately US $ 250.00 for the 20 sessions. The cost and time investment, compare favorably with those of counseling and, depending of specific circumstances, with pharmacotherapy. The major drawback is the initial cost of the Neotonus system which would be prohibitive for the exclusive use of treating men with PE outside a highly specialized sexual dysfunction facility serving men with the common complaint of PE. For those already using for other applications (urinary incontinency, pelvic pain syndrome), it could find another application.

This study carries all the limitations of a small pilot study, namely small patient population, limited follow up and a single therapeutic approach. The improvement in IVELT noted by several patients, in the absence of a control arm, could be ascribed to a placebo effect. Not investigated options such as a more intense regimen of FMS, longer treatment periods and combination with other modalities remain to be explored. The lack of invasiveness and systemic effects of FMS are definite advantages but only a placebo controlled study will provide definitive answers.

In conclusion, FMS shows some preliminary efficacy in patients with PE. Its lack of invasiveness and systemic effects makes FMS attractive but the ultimate proof of its value will reside in the couples' satisfaction and the prolongation of IVELT. The need for a randomized study is of fundamental importance to establish the place of the technique in the armamentarium. □

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