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Original Research

A novel on-demand therapy for lifelong premature ejaculation using a miniature transperineal electrical stimulator—the vPatch: an as-treated analysis

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Abstract

Background: While premature ejaculation (PE) is a common and disturbing sexual dysfunction in men, current available treatment modalities have limited efficacy and low treatment adherence.

Aim: To assess the feasibility, safety, and efficacy of the vPatch, a miniaturized on-demand perineal transcutaneous electrical stimulation device for treating PE.

Methods: This prospective bicenter international first-in-human clinical study consisted of 2 arms, was sham controlled, and had a randomized double-blind design. In terms of statistical power calculation, 59 patients aged 21 to 56 years (mean ± SD, 39.8 ± 9.28) with lifelong PE were included. During the initial visit, intravaginal ejaculatory latency time (IELT) was measured over a 2-week run-in period. Eligibility was confirmed in visit 2, based on IELT values, medical and sexual history, and patients' individualized sensory and motor activation thresholds during perineal stimulation with the vPatch. Patients were randomized to the active (vPatch) and sham device groups in a 2:1 ratio, respectively. The vPatch device's safety profile was determined by comparing the incidence of treatment-emergent adverse events. During visit 3, IELTs, Clinical Global Impression of Change scores, and Premature Ejaculation Profile questionnaire outcomes were recorded. Primary end points assessed vPatch device efficacy as mean change in geometric mean IELT; each person was compared with himself, with and without the device, and the sham group was compared with the active group.

Outcomes: Outcomes included changes in IELT and Premature Ejaculation Profile before and after treatment, last visit Clinical Global Impression of Change scores, and vPatch safety profile.

Results: Of 59 patients, 51 completed the study: 34 in the active group and 17 in the sham group. The baseline geometric mean IELT significantly increased from 67 to 123 seconds ($P < .01$) in the active group, as compared with an insignificant increase from 63 to 81 seconds ($P = .17$) in the sham group. The increase in mean IELT in the active group was significantly higher than in the sham group (56 vs 18 seconds, $P = .01$). IELT significantly increased by 3.1 times in the active vs sham group. The mean ratio of fold change (active:sham) was 1.4, significantly different from 1.0 ($P = .02$). No serious adverse events were reported.

Clinical Implications: Therapeutic use of the vPatch during coitus may become an on-demand, noninvasive, and drug-free treatment for PE.

Strengths and Limitations: To our knowledge, this is the first rigorous study investigating whether transcutaneous electrical stimulation during coitus could improve the symptoms of men with lifelong PE. The study is limited by the small number of patients, the exclusion of patients with acquired PE, the short-term follow up, and the use of a device based on a theoretic mechanism of action.

Conclusion: We demonstrated the possibility to treat lifelong PE by prolonging coitus on demand, using electric stimulation of ejaculation muscles with the vPatch.
Clinical trial registration: NCT03942367 (ClinicalTrials.gov).

Keywords: drug free; electrical muscle stimulation; medical device; noninvasive; premature ejaculation; sexual dysfunction; therapy; transcutaneous electrical stimulation.

Introduction

Premature ejaculation (PE) is a common and disturbing sexual complaint affecting 20% to 30% of sexually active men, according to type and definition by professional associations.[1-4] PE is associated with detrimental psychological, physical, and social effects,[5] yet its etiology remains unclear.[6,7] Currently, dapoxetine is the only oral compound developed for treating PE.[8,9] Although approved by the European Medical Agency, dapoxetine is not approved by the US Food and Drug Administration due to its undetermined efficacy and safety.[10-12] This shows the need for an effective and safe solution for PE.

Ejaculation is a complex reflex with 2 phases: emission and expulsion, both involving several pelviperineal anatomic structures.[13] Emission is the advancement of semen into the posterior urethra as a result of epithelial secretion and smooth

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muscle cell contractions around the epididymis and ductus deferens, propelling the sperm into the prostate and proximal urethra. Expulsion is a spinal cord reflex, which causes the ejection of sperm from the posterior urethra to the meatus. During this phase, smooth muscle bundles contract at the level of the bladder neck to prevent backflow of semen into the bladder, and the pelvic floor striated muscles (mainly the bulbospongiosus and ischiocavernosus) rhythmically contract to propel semen distally throughout the bulbar and penile urethra and toward the meatus.[14-16] These muscles have a major functional role in forcefully and rhythmically expelling semen from the meatus outward.

Gruenwald et al[17] proposed treating PE by transient inhibition of bulbospongiosus muscle contraction by neuromuscular transcutaneous electrical stimulation (TES). TES delivered to the neuromuscular junction may maintain approximately 80% muscle contraction for several minutes before inflicting muscle fatigue, inhibiting rhythmic contractions during the neural ejaculatory stimulus phase that may result in a delayed ejaculatory latency time. In 2020, Shechter et al[18] demonstrated that TES significantly increased the ejaculatory latency time of patients with lifelong PE, using a self-stimulation methodology with a standard commercial neuromuscular electrical stimulation device.

This prospective international bicenter trial is the first on the efficacy and safety of a miniature transperineal electrical stimulator—the vPatch (Virility Medical Ltd)—in men with lifelong PE. This randomized sham-controlled trial was double-blind and conducted in a real-life setting, during coitus, and on demand. Objectives were to determine the safety and efficacy of the device in delaying orgasm, as determined by intravaginal ejaculatory latency time (IELT) and patient-reported outcomes.

Methods

This clinical study was conducted in 2 research centers—Rambam Health Care Campus (Neurourology Unit, Haifa, Israel) and Villa Donatello Hospital (Urology Unit, Florence, Italy)—between September 2019 and July 2020. The centers were chosen by their expertise in sexual health or experience with clinical trials. The trial, based on protocol CL-RE-03-01 (ClinicalTrials.gov: NCT03942367), was conducted in accordance with the International Conference on Harmonization Good Clinical Practice Guideline, the Declaration of Helsinki, and ISO 14155:20111. It was approved by both centers' institutional review boards and funded by Virility Medical Ltd, and patients provided written informed consent. The trial ended after achieving the preplanned sample size. Participants were recruited from the patients with PE who had been admitted to the outpatient clinics of the participating institutions. They were required not to use any erectogenic or ejaculation-delaying drugs, systemic or topical, from 1 month prior to study initiation.

Patients

Men eligible for randomization in the study were 18 to 60 years old, in stable heterosexual relationships, and diagnosed with lifelong PE as defined by the International Society for Sexual Medicine.[19] This includes the inability to delay ejaculation in all or nearly all vaginal penetrations; negative personal consequences, such as distress and frustration; IELT <2 minutes in at least 75% of cituses; and no attempts >3 minutes. Patients were asked to complete the Premature Ejaculation Diagnostic Tool (PEDT), a validated self-administered 5-item brief diagnostic measure to assess self-perceived PE,[20] and the erectile function domain of the International Index of Erectile Function (IIEF-5).[21] Patients with a PEDT score ≥11 and an IIEF-5 score >22 were included. Table 1 presents exclusion and inclusion criteria.

Device description

The vPatch device is a flexible, skin-adhering, battery-powered device with an electronic module and 2 electrodes (Figure 1). It is adhered to the perineal skin where, once activated, it delivers electrical stimulation transcutaneously to the perineal muscles, inducing continuous tonic muscle contraction. Due to its magnitude and proximity to the perineal skin, the bulbocavernosus muscle is probably affected the most Each patch was preconfigured for active or sham mode before packaging, according to patients' individual parameters as determined during visit 2.

Study design

Screening: visit 1

Following a thorough explanation and informed consent, eligible patients underwent baseline PE and erectile dysfunction assessment, including the PEDT and IIEF-5 questionnaires, and proceeded to a run-in period when they attempted sexual intercourse at least 4 times without the vPatch. Using a stopwatch, patients' partners timed the duration of each intercourse (penetration to ejaculation initiation), after which patients recorded data in a log book.

Treatment: visit 2

Step 1: conditioning to stimulation by delivering TES to patients' forearm muscles.

Step 2: using the vPatch to deliver stimulation at the perineum, incrementally increasing intensity to determine a patient's individual sensory and motor stimulatory thresholds.

The first sensation reported by the patients during incrementation of the current intensity was considered the "sensory threshold"; then, the intensity was gradually and continuously increased until the patients indicated the sensation of perineal muscle contraction, which was considered the "motor threshold." All subjects were instructed to immediately report any discomfort or pain during visit 2 and the subsequent home phase treatment.

An unblinded subinvestigator preconfigured and packed 4 patches to an active or sham package; each package and device appeared identical. The patients in the active group received devices preconfigured to their motor thresholds, while the devices for the sham group were preconfigured to patients' corresponding sensory threshold sensations. Thus, both groups received a perceived stimulation, and patients were not told which level of stimulation, whether motoric or sensory, is considered therapeutic. The preconfigured stimulation intensity could not be changed by the patients. The randomization was carried out in accordance with the protocol instructions, with investigators and patients blind to each patch's configuration.

Patients were randomized into active vs sham device treatment groups in a 2:1 ratio, respectively. Following visit 2, patients proceeded to the home phase period, when they attempted sexual intercourse at least 4 times with the vPatch, with partners timing the duration of each intercourse. Patients in both groups logged intercourse dates, duration, and safety data for the 4 home sessions.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Men aged ≥18 and ≤ 60 y	A history of cardiovascular disorders
Diagnosis of clinical PE or with self-perceived IELT < 3 min	A history of sexual dysfunctions other than PE
Stable, heterosexual, monogamous, sexual relationship for at least 3 mo at the time of enrollment	Have erectile dysfunction
Plan to maintain the relationship for the duration of the study	Any type of implanted pacemaker or defibrillator
At visit 2: 75% of IELT baseline measurement <2 min and 25% of measurement <3 min	Diabetes mellitus with peripheral neuropathy
PEDT ≥11 at time of enrollment	Any perineal dermatologic disease
IIEF-5 ≥22 at time of enrollment	Any perineal skin irritation or lesions
Patients understand the nature of the study and provide informed consent to participation	Any psychiatric major disease or relevant medication
	Any use of antidepressant therapy, topical anaesthetic agents, or sexual-related cognitive behavioral therapy for PE within the 4 wk before enrollment
	Past occurrences of ejaculation before intromission
	History of genital or anorectal neoplastic illness 2 y before enrollment
	A pregnant partner
	Patients who are participating or have participated in other clinical studies within the 30 d before the study enrollment
	Any medical condition where the use of the device may jeopardize the patient's safety per the investigator's discretion

Abbreviations: IELT, intravaginal ejaculatory latency time; IIEF-5, 5-item International Index of Erectile Function; PE, premature ejaculation; PEDT, Premature Ejaculation Diagnostic Tool.

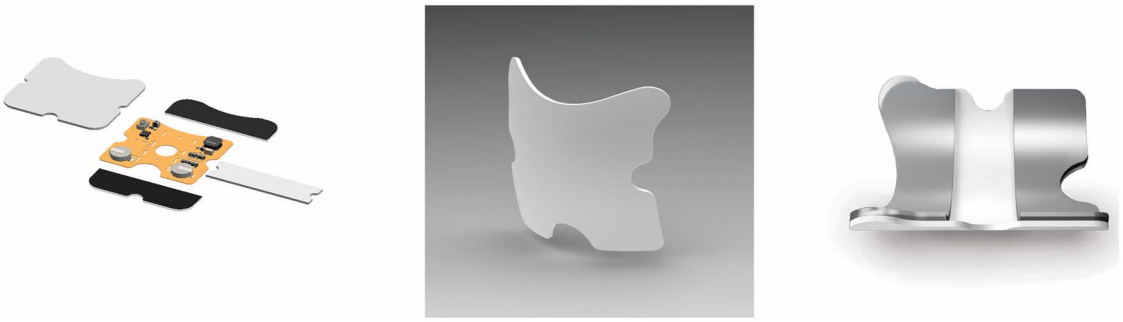

Figure 1. Device description. Left: Exploded view depicting the main components; Center: Front view; Right: Skin-side view.

Before and after treatment, patients completed the Premature Ejaculation Profile (PEP), a 4-item validated self-administered tool that includes measures of perceived control over ejaculation, satisfaction with sexual intercourse, ejaculation-related personal distress, and ejaculation-related interpersonal difficulties.[22]

Final visit: visit 3

For their final visit, patients returned to the site after 4 intercourse sessions, when they returned the used devices and filled out the PEP and Clinical Global Impression of Change (CGIC) questionnaires regarding their experience. The CGIC scale was applied as a measure of treatment response in men with PE.[23]

Statistical methods

End points

The primary end points assessed the vPatch's efficacy by mean change in geometric mean IELT (active vs sham treatment vs coitus without device) and the device's safety profile. Geometric rather than arithmetic mean IELT was selected for primary analysis, as IELT distribution often positively skews in PE populations with few very large IELT values.[24] Secondary efficacy end points included mean changes in arithmetic IELT, percentage of patients rating their PE as better or much better, mean change in ejaculation control or ejaculation-related personal distress, and percentage of patients achieving category 1 improvement from baseline to end of treatment in each PEP domain.

Randomization and blinding

Patients were assigned to active or sham groups in a 2:1 ratio, respectively, via a randomization schedule generated by SAS version 9.4 (SAS Institute Inc) and the eClinical OS electronic data capture system (IBM Ltd).

Randomization was achieved through permuted blocks of size 3, stratified by site. All sponsor and contract research organization personnel were blinded until the end of the study and database lock.

The 51 subjects provided a power of ∼80% (5% significance level), sufficient to detect a mean ± SD difference of 186.8 ± 218 seconds from baseline IELT. This also permitted defining the percentage of subjects reporting a positive impression of change (ie, CGIC), assuming change rates of 65% and 20% in the active and sham groups, respectively. Assuming a dropout rate of 15%, we planned to be recruit 60 subjects: 40 in the active group and 20 in the sham group. The

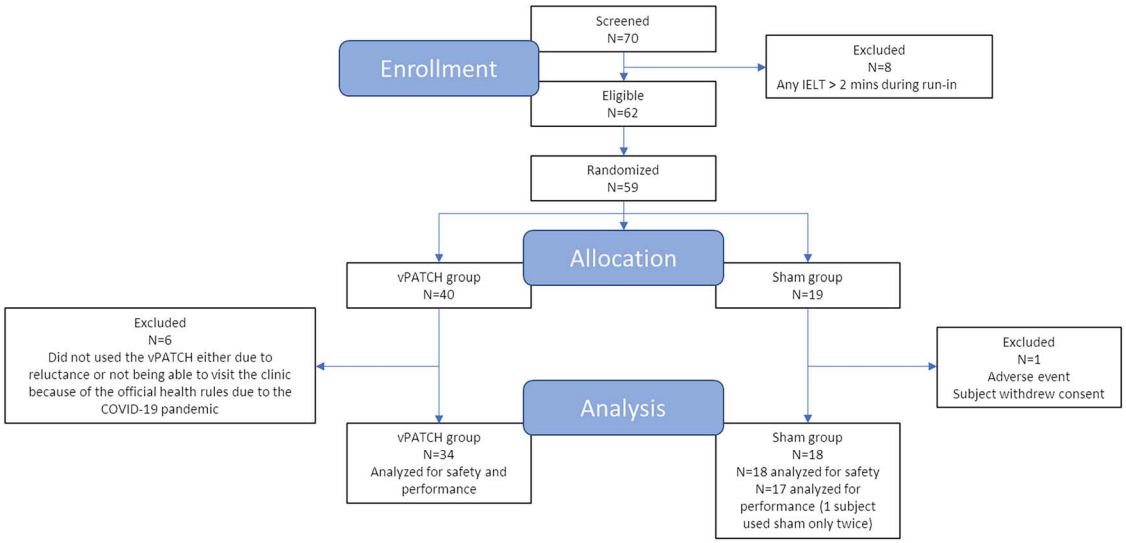

Figure 2. Patient disposition.

Table 2. Baseline demographic characteristics.

	Active (n = 34)	Sham (n = 17)	*P* value [a]
Age, y			.80
No.	40	19	
Mean (SD)	39.8 (9.28)	40.4 (9.69)	
Median [range]	40.5 [21-56]	40.0 [26-54]	
Height, cm			.05
No.	40	19	
Mean (SD)	178.8 (5.94)	175.7 (4.74)	
Median [range]	180.0 [165-190]	175.0 [168-187]	
Weight, kg			.50
No.	40	19	
Mean (SD)	81.0 (13.70)	78.5 (10.78)	
Median [range]	77.5 [56-120]	76.0 [64-110]	
Body mass index, kg/m^2			.91
No.	40	19	
Mean (SD)	25.3 (3.86)	25.4 (3.15)	
Median [range]	24.8 [16.5-35.1]	25.2 [22.1-35.9]	
Race: White, % (No.)	100 (40/40)	100 (19/19)	>.99 [b]

[a]Two-sided *t* test unless indicated otherwise. [b]Two-sided chi-square test.

patients, investigators, and statistician were all blinded to the study arms.

Statistical analyses

Statistical analyses were performed with SAS version 9.4 on the cohort treated with the vPatch during 3 or 4 coitus sessions. IELT was averaged by either arithmetic or geometric means and defined as baseline IELT.

For analysis of fold change in IELT over time, scores were transposed through natural logarithms. Change scores were then analyzed by mixed linear modeling via PROC MIXED, adjusted for treatment, age, and baseline IELTs as fixed factors and site as a random factor. Adjusted estimates of fold change for each treatment group, ratio of change, 95% CIs, and 2-sided *P* values were obtained. To analyze differences over time, scores from baseline were subtracted from those in the follow-up period, and a similar adjusted mixed linear model was used. Adjusted mean difference for each treatment, adjusted treatment effects (active – sham), 95% CIs, and 2-sided *P* values were obtained.

Results

Patient disposition

Of 70 men screened, 62 were eligible, of whom 59 were randomized and enrolled in the study (40 in the active group and 19 in sham group); 51 were eligible for results analysis (34 active and 17 sham). Excluded were 7 patients who never used the vPatch due to unexpected life circumstances (eg, road accident, partner related) and 1 who used the vPatch only 2 times. The rates of discontinuation were similar for both treatment groups (Figure 2).

Baseline patient characteristics

The mean patient age was 39.8 years in the active group and 40.4 years in the sham group; 22.5% (9/40) of subjects in the active group had previous medical conditions vs 31.6% (6/19) in the sham group ($P = .3$; Table 2). No abnormalities were found during physical examination, and all baseline characteristics were similar between the groups. Without treatment, the geometric mean IELTs were 67.2 and 63.4 seconds for the active and sham groups, respectively.

Table 3. Efficacy analysis: comparison of active vPatch and sham in mean increase in geometric and arithmetic IELT in seconds.

IELT	Active (n = 34)		Sham (n = 17)
Geometric			
Baseline, mean (SD), s	67.2 (34.82)		63.4 (30.72)
Treatment, mean (SD), s	123.3 (70.90)		80.8 (51.43)
Adjusted change from baseline, [a] mean (SE), s	55.8 (8.42)		18.0 (11.92)
Adjusted difference, active vs sham, mean [95% CI]		37.76 [8.35-61.17]	
P value		.01*	
Arithmetic			
Baseline, mean (SD), s	68.0 (34.68)		64.8 (30.66)
Treatment, mean (SD), s	127.4 (74.63)		84.9 (54.45)
Adjusted change from baseline, [b] mean (SE), s	59.1 (9.22)		20.6 (13.05)
Adjusted difference, active vs sham, mean [95% CI]		38.5 [6.3-70.7]	
P value		.02*	

Abbreviation: IELT, intravaginal ejaculatory latency time. [a]Change from baseline in geometric mean IELT over the treatment assessment period was analyzed via a mixed linear model (analysis of covariance) that included the following variables as fixed effects: treatment, baseline geometric mean IELT, and age as covariates and site as a random effect. [b]Change from base line in arithmetic mean IELT over the treatment assessment period was analyzed via a mixed linear model (analysis of covariance) that included the following variables as fixed effects: treatment, baseline arithmetic mean IELT, and age as covariates and site as a random effect. $^*P < .05$.

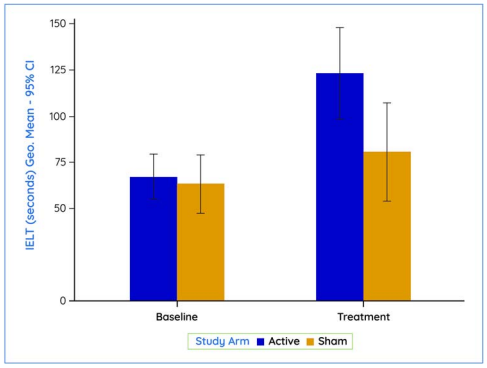

Figure 3. Mean geometric intravaginal ejaculatory latency time (IELT) at baseline and during treatment.

Self-perceived degrees of distress from PE, as reported in the PEDTs, were similar in the active and sham groups (16 and 15.9, respectively, $P = .91$). No patients in either group experienced erectile dysfunction, as indicated by their IIEF-5 scores (24.5 and 24.6, $P = .69$). No statistical differences were found between the groups in all 4 domains of the PEP questionnaire at baseline.

Efficacy analysis

IELTs

Presented are means and 95% CIs for IELTs at baseline and during treatment, geometric mean IELTs for each patient at baseline, and changes from baseline during treatment (Table 3, Figures 3 and 4). The coordinates of the y- and x-axes respectively show the magnitude of IELT improvement vs baseline for each patient. IELTs did not improve in most sham group patients but improved significantly in most active group patients.

The primary end points of the geometric mean increase in IELT from baseline was 56 seconds in the active group, which was significantly different from and 3.1 times greater than the geometric mean increase of 18 seconds in the sham group ($P = .01$). The geometric mean fold increases in IELTs were 1.7 and 1.2 for the active and sham groups, respectively. After adjustment for baseline IELT, site, and treatment, the mean ratio of fold change (active/sham) was 1.4, significantly different from 1.0 ($P = .02$).

Our data confirmed the clinically significant efficacy of vPatch therapy. For example, based on an approach previously used in the literature for calculating arithmetic mean fold changes in IELT, fold changes were 2 vs 1.4 for the active and sham groups, respectively. Clinically and statistically significant treatment-related changes in IELT differences from baseline were found to favor the vPatch.

Patient-reported outcomes

At the end of the study CGIC questioner was completed, 73.5% (25/34) of subjects using the active vPatch had a clinical global impression of improvement in the degree of their PE, as opposed to only 41.1% (7/17) of those who used the sham device ($P = .03$) ; that is, 78.6% more subjects using the vPatch cited improvement (Table 4).

Premature Ejaculation Profile

More active group patients improved their scores for all 4 PEP questions as compared with those randomized to placebo. Improvements in perceived control over ejaculation, personal distress, interpersonal difficulty related to ejaculation, and satisfaction with sexual intercourse were significantly higher posttreatment than baseline in the active group ($P < .0001$ in all PEP parameters) but were not significant in the sham group ($P = .17$, .27, .09, and .17, respectively). Improvement in PEP was significantly higher in the active group than the sham group, except for sexual intercourse satisfaction ($P = .01$, .04, .01, and .11).

The geometric means of the IELT were calculated per period (baseline or treatment) for each subject who positively responded to the treatment. A subgroup analysis of subjects with any improvement in IELT showed that 91% (31/34) in the active group showed improvement in IELT during the treatment period as compared with baseline. The mean time fold in IELT for responders was 2.04 with a 95% CI of 1.68 to 2.40.

Safety analysis

No serious or severe treatment-emergent adverse events (AEs) were reported. Two minor AEs occurred in the active group, both related to the study device. The AEs occurred in 2 of 186 sessions (52 at visit 2, 134 during treatment); therefore the AE was 1.1% in the active group vs 0.0% (0/70) in

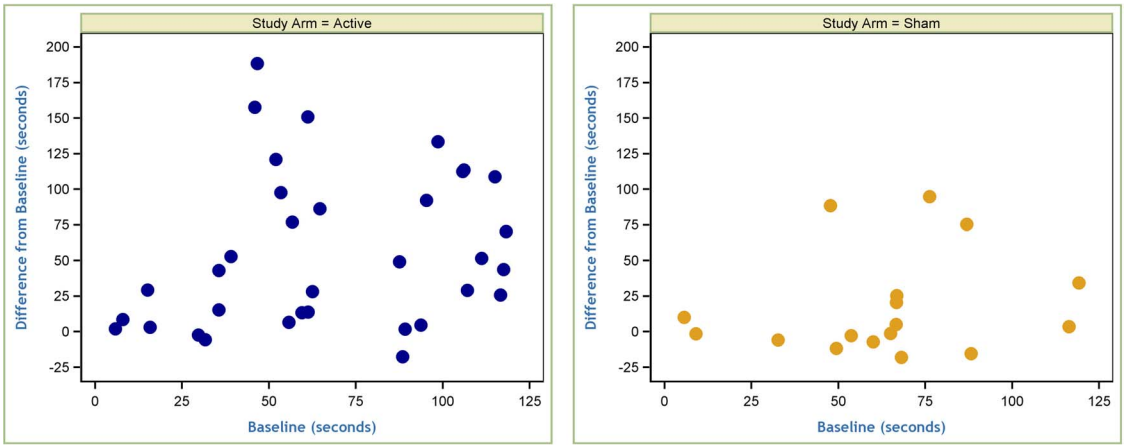

Figure 4. Difference from baseline in geometric mean intravaginal ejaculatory latency time (IELT) by arm per subject.

Table 4. Patient-reported outcomes.

	Active		Sham
Any improvement in CGIC			
% (No.)	73.5 (25/34)		41.2 (7/17)
95% CI, %	55.64-87.12		18.44-67.08
P value[a]		.03*	
PEP			
Perceived control over ejaculation			
Before treatment, mean (SD)	0.9 (0.6)		0.8 (0.8)
After treatment, mean (SD)	2.1 (1.0)		1.3 (0.8)
Adjusted change from before,[b] mean (SE)	1.2 (0.2)		0.3 (0.3)
Adjusted difference, active vs sham, mean [95% CI]		0.9 [0.3 to 1.4]	
P value		.01*	
Satisfaction with sexual intercourse			
Before treatment, mean (SD)	1.6 (1.02)		1.0 (0.94)
After treatment, mean (SD)	2.4 (1.18)		1.6 (1.06)
Adjusted change from before,[b] mean (SE)	0.9 (0.20)		0.4 (0.26)
Adjusted difference, active vs sham, mean [95% CI]		0.5 [−0.1 to 1.2]	
P value		0.11	
Personal distress related to ejaculation			
Before treatment, mean (SD)	1.3 (0.84)		1.5 (1.18)
After treatment, mean (SD)	2.4 (1.16)		1.7 (0.92)
Adjusted change from before,[b] mean (SE)	1.1 (0.20)		0.4 (0.28)
Adjusted difference, active vs sham, mean [95% CI]		0.7 [0.0 to 1.4]	
P value		.04*	
Interpersonal difficulty related to ejaculation			
Before treatment, mean (SD)	−0.1 (0.35)		0.0 (0.00)
After treatment, mean (SD)	1.5 (1.28)		0.5 (0.87)
Adjusted change from before,[b] mean (SE)	1.5 (0.21)		0.5 (0.31)
Adjusted difference, active vs sham, mean [95% CI]		0.9 [0.2 to 1.7]	
P value		.01*	

Abbreviations: CGIC, Clinical Global Impression of Change; PEP, Premature Ejaculation Profile. [a]Two-sided Cochran-Mantel-Haenszel test controlled for site. [b]Adjusted means and their differences are extracted from a linear regression model (analysis of covariance). Change from baseline at the end of the treatment assessment period was analyzed via a linear model that included the following variables as fixed effects: treatment, baseline value, age, and site as covariates. $^{*}P < .05$.

the sham group ($P > .99$). One subject cited "discomfort due to device vibration in inguinal scar site," and another indicated "pain and discomfort during sexual intercourse in pelvic area"; however, both continued participating in the study.

Discussion

The accumulated knowledge of TES effects on human tissue, specifically muscle activation, led us to initiate a series of studies applying TES to pelvic floor muscles and later to use the newly developed vPatch for treating PE. Essentially, when a muscle undergoes continuous stimulation, the series of successive contractions can prevent muscle relaxation and thus maintain a mild contractile tonus. Applying TES to these muscles during coitus may therefore keep them in sustained contraction for several minutes, which may require a higher central or autonomic stimulatory threshold for initiating the natural rhythmic muscle contractions necessary to complete ejaculation.

Pastore et al[25] demonstrated that rehabilitation treatments with electrical stimulation delivered to the pelvic floor can treat lifelong PE. Furthermore, TES results obtained in our previous study with a self-stimulation protocol[18] revealed that on-demand electrical stimulation can effectively and safely treat patients with lifelong PE, without their having prior training, significantly increasing ejaculatory latency time. Clinically, in patients with PE, this intervention may be expressed by a significant increase in latency time to ejaculation.

To our knowledge, this is the first rigorously designed study to investigate whether TES could improve symptoms in men with lifelong PE. This randomized double-blind clinical trial demonstrated the potential of the vPatch, a miniaturized TES device, to successfully treat symptoms of lifelong PE. Statistically significant differences were found between the active and sham devices on fold changes in (1) geometric and arithmetic mean IELT; (2) PEP questions on perceived control, personal distress, interpersonal difficulty, and satisfaction; and (3) CGIC. The vPatch was feasible and safe, with rare and minimal nonserious side effects and significant beneficial effects in delaying ejaculation.

We demonstrated that ejaculation was delayed after applying the vPatch to the pelvic floor muscles, probably by temporarily increasing muscle tone and consequently ejaculatory control in patients with PE. When stimulation ceased, the muscles regained their typical capacity. Since treatment with the vPatch is on demand during coitus and not typically on a daily basis, muscle tolerance to stimulus is not expected to develop. To the contrary, it can be speculated that after use of the vPatch several times a week, muscle strengthening is expected, which together with the positive psychological effect of coitus prolongation may reduce the severity of patients' PE without use of the vPatch. Of course, further long-term studies and follow-up are required to test this hypothesis.

To the best of our knowledge, no published literature has identified a meaningful and clinically significant threshold response to intervention in men with lifelong PE. Statistical superiority to baseline or placebo outcome measures is not always associated with a clinically significant response. Intervention success can be measured as the point when IELT fold is associated with significant reduction in personal distress. Clinically important, an overall significant increase in geometric mean IELT was found with use of the vPatch for the active group vs the sham group. Additionally, perceived control over ejaculation, personal distress related to ejaculation, and interpersonal difficulties related to ejaculation questions received significantly higher scores from subjects using the active vPatch vs the sham. At the end of the study, significantly more subjects using the vPatch (50% difference) had a clinical global impression of improvement in the degree of their PE as compared with those who used the sham device.

The power analysis for the change in IELT was based on the coefficient of variation (ratio between the SD and the mean) and not on the mean difference in change from baseline. In addition, it is common practice to calculate the sample size needed, based on a *t* test, while the final analysis uses a more powerful statistical test, such as a mixed model. Therefore, since the coefficient of variation was not dramatically higher and as we used a more powerful test, the study was not underpowered.

Our study is limited by the small number of patients, the exclusion of patients with acquired PE, the short-term follow-up, and the use of a device based on a theoretic mechanism of action. Unfortunately, of the initially randomized patients, 7 could never use the vPatch due to unexpected life circumstances (eg, road accident, partner related, COVID-19 restrictions), and 1 used the vPatch only 2 times (before his wife had a chronic health problem). Moreover, the 2-fold increase that was established with the vPatch may not be sufficient for patients whose IELT is very short (eg, 15-30 seconds). Of note, PE treatments currently approved by the European Medicine Agency (ie, dapoxetine and Fortacin [lidocaine and prilocaine]) have similar ejaculation-delaying efficacy, with more significant side effects.[26] Nevertheless, the conclusive results establish a basis for further investigations in a larger group of patients through a wider inclusion protocol.

Whether indicated for PE or off-label, selective serotonin reuptake inhibitors have a low rate of acceptance by patients, mainly due to the lack of spontaneity involved and to the significant rates of AEs caused by the treatment.[9-11] Thus, new treatment modalities, such as on-demand electrical stimulation, may provide much safer, immediate, and significant beneficial effects that meaningfully improve the sexual well-being of couples in which the man suffers from PE.

Conclusion

There are very few options for treating PE, and although this is a new and ongoing investigation, results are promising. We demonstrated that TES delivered by the vPatch device was well tolerated and resulted in significant benefits in objective and subjective measures of ejaculatory control in men with lifelong PE. This treatment modality offers potential as an on-demand drug-free modality for treating PE.

Supplementary material

Supplementary material is available at *The Journal of Sexual Medicine* online.

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Conflicts of interest: A.S. is a consultant for Virility Medical Ltd and received compensation. A.S. was granted the option to purchase equity of Virility Medical Ltd. T.G. is an employee of Virility Medical Ltd and a shareholder. I.G. is a consultant for Virility Medical Ltd and received compensation. I.G. was also granted the option to purchase equity of Virility Medical Ltd. E.C.S. is a consultant for Virility Medical Ltd and was granted the option to purchase equity. B.A., F.D. FD is a consultant for Virility Medical and received compensation, N.M. declare no conflicts of interest.

Data availability

Data are not available to other researchers due to the privacy concerns for this vulnerable population. If requested, the corresponding author will provide the data or will cooperate fully in obtaining and providing the data on which the manuscript is based for examination by the editors or their assignees.

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