Medical Hypotheses 109 (2017) 181–183

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy

Transcutaneous neuromuscular electrical stimulation may be beneficial in the treatment of premature ejaculation

Ilan Gruenwald[a], Ege Can Serefoglu[b], Tal Gollan[c], Shmuel Springer[d], Gideon Meiry[c], Boaz Appel[a], Arik Shechter[a,e,*]

[a] Neurourology Unit, Rambam Healthcare Campus, Haifa, Israel
[b] UroKlinik, Istanbul, Turkey
[c] Virility, Israel
[d] Physical Therapy Department, Faculty of Health Sciences Ariel University, Israel
[e] Department of Family Medicine, Ruth and Bruce Rappaport Faculty of Medicine, Technion Institute of Technology, Clalit Health Services, Haifa, Israel

ABSTRACT

Approximately 20–30% of sexually active men suffer from Premature Ejaculation (PE), but the pathophysiology still remains unclear and the current available treatments for PE are unsatisfying. Considering the role of rhythmic bulbospongiosus and ischiocavernosus Muscles contractions on the ejaculatory reflex, we hypothesize that weakening this muscles via inhibiting it's contractions by Application of Neuromuscular Electrical Stimulation prior to the planned sexual activity, may have a beneficial effect in the treatment of PE. Using miniaturized perineal on-demand stimulation device, in a home setting during sexual intercourse may become the first line of treatment for PE.

Introduction

Premature ejaculation (PE) is a very common and disturbing sexual dysfunction in men, associated with detrimental psychological, physical and social effects. Approximately 20–30% of sexually active men suffer from PE (Porst et al., 2007; [1–3]). Although this dysfunction has been widely investigated, its pathophysiology still remains unclear. Today, there is only one oral compound, which has been specifically developed for the pharmaceutical treatment of PE, Dapoxetine. Although it has been approved by the European Medical Agency (EMEA), Dapoxetine has not been approved by the U.S. Food and Drug Administration (FDA), due to its controversial efficacy and safety (Mondaini et al., 2013; [4, 5]). Therefore, the treatment of PE continues to be a major area of medical research.

Physiology of ejaculation

From the physiologic point of view, ejaculation has two phases: emission and expulsion, which involve several pelvi-perineal anatomical structures. After a sufficient erotic stimulus, a tight coordination of sympathetic, parasympathetic and somatic divisions of the nervous system is necessary for a normal ante grade ejaculation [6].

Emission is the ejection of semen into the posterior urethra, as a result of epithelial secretion and smooth muscle cell contraction [7]. All of the organs contributing to emission phase receive a dense autonomic innervation composed of both sympathetic and parasympathetic axons, which are mainly derived from the pelvic plexus. Epididymis, vas deferens, seminal vesicles, prostate gland, prostatic urethra and bladder neck are all involved in the emission phase [6].

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 in the bladder neck to prevent backflow of semen into the bladder, and the pelvic floor muscles, with bulbospongiosus and ischiocavernosus muscles playing major functional roles, display significant rhythmic contractions to propel semen distally, throughout the bulbar and penile urethra towards the meatus [8,9].

Definition and pathophysiology of PE

The exact definition, epidemiology, classification and pathophysiology of PE have been dispersed over time [10]. In the recent years, there has been some progress in PE research, which resulted in a better understanding and study of this prevalent condition [11]. Several professional organizations such as the American Psychiatric Association (APA) and the International Society for Sexual Medicine (ISSM) have revised their PE definitions considering the recent evidence pertaining

* Corresponding author.
E-mail address: arikshec@gmail.com (A. Shechter).

http://dx.doi.org/10.1016/j.mehy.2017.10.008
Received 20 July 2017; Accepted 7 October 2017

to PE [12,13]. Considering the key elements (time, control and distress) in these evidence-based definitions, PE can be defined as: 1) An ejaculation that occurs at less than 1 min from vaginal penetration (primary or lifelong PE) or less than 3 min (secondary or acquired PE); and 2) ejaculation that cannot be postponed in nearly all attempts with vaginal penetration; and 3) PE inflicts personal distress with negative consequences such as avoidance of sexual relations [13].

It is well accepted in modern sexology, that within reasonable limits, if a patient experiences dissatisfaction and distress as a result of inability to control the timing of orgasm, he is eligible to medical assistance, regardless of his objective latency time.

The mechanisms, which play role in the pathophysiology of PE, have not yet been completely elucidated. Hyposensitivity and/or hypersensitivity of the central serotonin receptors [14], genetic factors [15], endocrinologic disruptions [16] and some urologic conditions [17,18] may be responsible for the hyperactivity of the ejaculation reflex. In addition to these organic disorders, psychological problems (e.g. performance anxiety, relationship problems and etc.) may cause acquired PE [19] by activating the sympathetic nervous system and causing reduced ejaculatory threshold [20].

Treatment of premature ejaculation

In the past, the origin of PE was attributed mainly to psychological factors; nevertheless, possible neurobiological aetiologies were recently proposed [21]. These advancements revolutionized the PE treatment and currently pharmacotherapy is considered as the most effective treatment in PE [22]. Until recently only chronic selective serotonin reuptake inhibitors (SSRIs) confirmed their role as first-line agents with their consistent efficacy in delaying ejaculation [23]. However, only Dapoxetine (Priligy, Menarini, Italy), which is a short acting SSRI, has been approved for the treatment of PE [24]. Unfortunately, recent post-marketing studies demonstrated that discontinuation rate of Dapoxetine is very high [4,25] due to its limited efficacy and side effects [26]. Therefore, several new compounds are being investigated as an alternative for PE treatment.

Considering the role of rhythmic bulbospongiosus muscle contractions on the ejaculatory reflex, Serefoglu and Silay hypothesized that weakening this muscle via botulinum toxin injections may delay the time of ejaculation [27]. In an animal study, botulinum-A toxin injection into the bulbospongiosus muscle is shown to be effective in extending the ejaculatory latency without affecting the ability to engage in sexual activity or achieve ejaculation [28]. Although clinical studies which demonstrate the efficacy and safety of this treatment modality in men with PE are being conducted, their results have not been published yet (ClinicalTrials.gov Identifier: NCT01917006).

Transcutaneous neuromuscular electrical stimulation

Neuromuscular electrical stimulation (NMES) involves the application of a series of intermittent stimuli to superficial muscles, with the main objective to trigger muscle contractions due to the activation of the intramuscular nerve branches [29]. Transcutaneous NMES is a common and well-recognized treatment to improve muscle function [29].

Eriksen and Mjølnerød [24] defined pelvic floor NMES as the activation of the pudendal nerve afferents, which results in contractions of the smooth and striated muscles in the pelvic floor. The efficacy of pelvic floor muscle training using transcutaneous NMES in many urological problems (e.g. lower urinary tract symptoms, urinary incontinence, erectile dysfunction and premature ejaculation) has been demonstrated [30–32]. These studies revealed that contraction of the male pelvic floor muscles (i.e., bulbospongiosus and ischiocavernosus) via NMES can be safely performed for several minutes, with good perception and without discomfort [27,28].

Hypothesis

As ejaculation involves rapid stereotyped rhythmic contractions of the bulbospongiosus and ischiocavernosus muscles, inhibiting this type of contractions may have a beneficial effect in the treatment of PE. When a muscle is continuously stimulated the successive contractions fuse together resulting in inability of muscle relaxation. Application of NMES to these muscles prior to the planned sexual activity may keep them in a sub-tetanic sustained contraction for several minutes, which may inhibit the natural rhythmic muscle contractions, which is necessary for the completion of the ejaculatory process. This intervention may significantly increase the time to ejaculation in patients with PE.

However, there are some limitations of our hypothesis. Though the carry-over effect (i.e., increased ejaculatory latency time) of NMES to improve the contractile strength of these muscles has been reported after a repetitive treatment [33], the immediate on-demand effect of NMES during sexual intercourse has not been demonstrated yet. Thus, a well-designed clinical study is necessary to establish this effect. Another important issue of such study should be to reject the undesirable probability of anejaculation which might be characterized by the absence of ejaculation due to the spastic contraction of these muscles. Furthermore, a technical factor that needs to be considered is the ability of the subject to accurately position the electrodes in the correct place in the perineum in order to achieve the desired outcome of delaying the ejaculation. Hence, future studies should evaluate the effectiveness of this on demand treatment in comparison with other commonly used treatments.

We believe that the new on-demand application of NMES on the perineum skin may be a viable, efficient and safe treatment option for PE, if the efficacy of this therapy will be proven by future studies, we suggest to develop a transcutaneous electrical stimulation miniature device for the treatment of premature ejaculation.

Conflict of interests

Gruenwald Ilan – consultant for Virility Medical, a company that intends to develop a device based on this hypothesis.

Ege Can Serefoglu – consultant for Virility Medical, a company that intends to develop a device based on this hypothesis.

Tal Gollan – CEO of Virility Medical, a company that intends to develop a device based on this hypothesis.

Shmuel Springer – consultant for Virility Medical, a company that intends to develop a device based on this hypothesis.

Gideon Meiry – consultant for Virility Medical, a company that intends to develop a device based on this hypothesis.

Boaz Appel – Non.

Arik Shechter – consultant for Virility Medical, a company that intends to develop a device based on this hypothesis.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.mehy.2017.10.008.

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