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ORIGINAL ARTICLE

Comparing the effectiveness of functional electrical stimulation via sexual cognitive/behavioral therapy of pelvic floor muscles versus local injection of botulinum toxin on the sexual functioning of patients with primary vaginismus: a randomized clinical trial

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Abstract

Introduction and hypothesis Most patients suffering from vaginismus feel sinful, anxious, and incompetent, with reduced self-confidence. This study was aimed at comparing the effectiveness of the physiotherapy of pelvic floor muscles as a standard treatment and local injection of botulinum toxin on the sexual functioning of patients with primary vaginismus.

Methods In this randomized clinical trial (RCT), the study population included women with primary vaginismus referred to the Sexual Health and Gynecologic Clinics of Imam Khomeini Hospital during 2013–2014. They were diagnosed according to DSM-5 criteria and underwent treatments with botulinum injection (intervention group) and physiotherapy as the current treatment (control group). The participants' primary and secondary outcomes were measured based on successful intercourse and sexual functioning of each group.

Results The results indicated that the overall standard physiotherapy, along with other measurements, such as functional electrical stimulation and desensitization, could effectively improve the patients' Female Sexual Function Index compared with botulinum treatment. At the end of the study, it was found that 20 and 26 patients out of the 30 and 28 patients in the intervention and control groups managed to have successful intercourse respectively ($P = 0.014$). Also, sexual dysfunction frequencies were seen to be decreased by 26.6% and 50% in the mentioned groups respectively ($p = 0.008$ and $p < 0.001$).

Conclusions Considering the higher efficacy of physiotherapy procedures compared with those of the desensitization and electrical stimulation techniques, this therapeutic method should be considered the first-line treatment of vaginismus (IRCT2016061828486N1).

Keywords Lifelong vaginismus · Botulinum toxin · Sexual function · Physiotherapy · Functional electrical stimulation

Introduction

Vaginismus is referred to as having a persistently or recurrently painful vagina on entry of a penis, fingers, or other objects into it [1]. Recurrent or persistent spasm of the vaginal musculature interfering with vaginal penetration constitutes a barrier to intercourse and causes considerable discomfort or interindividual difficulties [2]. The available data show that spasm

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is not always associated with vaginismus [3]. This condition may occur as a consistent problem in intercourse even when a woman has already expressed consent or tries to enter something into the vagina. This can make sexual intercourse impossible and lead to great pain in the severest cases. With this dysfunction, intercourse is usually impossible and leads to an unconsummated marriage [4, 5]. The inability to have sexual intercourse due to vaginismus can affect marital relationships by causing poor confidence in couples, the building of outside-home relationships, and leading to infidelity and divorce [6]. Paying attention to this disorder is very important because sexual behavior is a response to an instinctive motivation and is necessary for the continuity of generation, and can lead to enormous consequences in a couple's emotional and sexual lives. Due to the lack of awareness in society, patients suffering from vaginismus consider themselves defective and thus continuously blame themselves. Most affected patients feel sinful, anxious, and incompetent, and have reduced self-confidence [7–9]. Owing to the differences in the diagnostic criteria for this disorder, various studies have reported different estimates of its prevalence and incidence [10]. In a recent study conducted in 28 provinces of Iran, its prevalence among 20- to 60-year-old women has been estimated to be 26.7% [11], whereas its overall prevalence in the world has a range of 5–20% [12, 13].

In past years, different etiologies for vaginismus have been mentioned in various studies. Primary studies have considered a mental defensive mechanism for insoluble contradictions during childhood as the cause of this problem, but in the past three decades, special attention has been paid to somatic/mental causes, including pain expected at the first sexual experience and the resulting fear, religious prejudice, and feeling sinful in a sexual affair, lack of correct sexual education and the resulting negative beliefs, anxiety disorders, sexual abuse in childhood, infections, and organic disorders, such as hymen anomaly, endometriosis, and vaginal atrophy [14–16]. Several cognitive and behavioral factors, in addition to the physical aspects of vaginismus, have led to the suggestion of various treatments for this disorder, including muscular spasm relief by vaginal dilation via desensitization, and different relaxation methods [17], correct sex education aimed at the promotion of sexual knowledge and positive attitudes [18], elimination of patients' mental problems, such as fear of pain and a negative subjective image of the body or genital area through psychotherapy or sex therapy [19], biofeedback methods and desensitization [20], local injection of botulinum toxin [21], physiotherapy of pelvic floor muscles [22, 23], and use of local anesthesia cream [24]. Because of the use of different treatment methods for vaginismus and the achievement of varied efficiencies of interventions, no standard method has been proposed for the intervention. The aim of this study was to compare the effectiveness of relaxation exercises, functional electrical stimulation (FES), desensitization, and sensational focus of pelvic floor (levator ani) muscles as a routine intervention (physiotherapy) and the local injection of botulinum toxin into those muscles on the sexual functioning of patients with vaginismus.

Materials and methods

This randomized clinical trial was based on a parallel design of a one-to-one ratio for the groups of local botulinum toxin injection and physiotherapy treatment, which were conducted in Imam Khomeini Hospital, Tehran (Registration code IRCT2016061828486N1 presented at www.irct.ir). The study population of this research included women with vaginismus referred to the Sexual Health and Gynecologic Clinics of Imam Khomeini Hospital during 2013–2014. They were diagnosed based on DSM-5 criteria and underwent physiotherapy as the current treatment (control group) or botulinum injection (intervention group). The study population consisted of 74 patients aged 20–40 years, who had primary vaginismus of grade III or IV based on Lamont categorization.

According to the Lamont categories, vaginismus is divided into four grades [25]. The first grade includes spasms of levator and perineal muscles that are resolved when the physician gives confidence to the affected patients to allow subsequent examinations. The second grade includes a generalized spasm of the pelvic floor muscles, which is defined as the presence of contracted and painful muscles upon palpation and elevated resting pressure during vaginal manometry [26] to the extent where the patient would not allow any examinations. The third grade includes severe spasm of the pelvic floor muscles associated with elevating the buttocks during examination. The fourth grade is defined as the severest spasm, along with elevating the buttocks and legs during examination [25]. To the best of our knowledge, there are no available data on the reliability and validity of this widely used method of classification [8, 27, 28].

The inclusion criteria consisted of nonpregnant women aged 20–40 years, who had been referred to the Sex Health and Gynecologic Clinics of Imam Khomeini Hospital between April 2013 to March 2014 and who were diagnosed to have primary vaginismus of Lamont grade III or IV. The exclusion criteria included lacking the appropriate cooperation for treatment and follow-up procedure and having any contraindications to receiving botulinum, including allergies to albumin, botulinum toxin, or its injection components, a previous history of treatment with botulinum or physiotherapy, infection at the injection site, and diseases involving nerves and muscles, such as myasthenia gravis and Lambert–Eaton syndrome, vulvodynia, cutaneous problems at the vulva or perineum, anal fissure, urinary duct or rectum disorders, and coagulation disorders urging them to use anticoagulation drugs.

In the present research, a balanced block randomization method was employed with four blocks to randomly divide the patients into the intervention and control (conventional treatment) groups. The desired sample size was created by applying STATA software to generate a chain of random numbers from 1 to 6. Assuming six modes for the total number of cases to fit two people in four blocks, any numbers exceeding 6 would result in the regeneration of the next number regardless of the previous number. Then, a person who was not involved in the design was employed to prepare random allocation sequences for the cases under study, put them in sealed (airtight) envelopes, and choose a five-digit serial number for them. The participants were assigned to the intervention (botulinum toxin) and control (traditional physiotherapy treatment) groups after completing their basic information and examinations and immediately opening all the serially and randomly numbered envelopes ($n = 74$). It should be said that the patients could not be notified about each other's treatment processes, as there were few qualified referrals based on the study's inclusion criteria, while the treatment groups were unaware of the study hypothesis and were followed at two different places. Moreover, the responsible agents had the same situations as the patients and provided the treatments according to the different locations considered.

The primary and secondary outcomes of this investigation were measured based on successful intercourse and sexual functioning in each group respectively [29]. Sexual dysfunction would be defined to be present if a woman had a total score of less than 26.55 based on the Female Sexual Function Index (FSFI). Sexual functioning of the women with vaginismus was measured in the two control and intervention groups via the FSFI questionnaire representing confirmed validity and reliability [29]. Pelvic organ prolapses were tested using the pelvic organ prolapse quantification system (POP-Q) test; as most of the participants in the study have not been pregnant, they had POP-Q stages 0 (92%) and 1 (8%).

The patients assigned to the intervention group received 500 units of botulinum diluted in 1.5 cc of normal saline associated with a total dosing of 150–400 units in their levator ani (puborectalis) muscles, which were injected at three points in both sides using a 23-gauge needle. In severe cases, 1–5 mg of midazolam and 50–150 mg of fentanyl were used for pain relief before injection. During the treatments, they were placed under an oxygen mask and evaluation of pulse oximetry. The primary dosing of botulinum began with 150–200 units, which were gradually increased to 400 units to prevent any probably unwanted reactions. They were discharged after injection in one session. In the group treated with physiotherapy (current treatment), relaxation exercises, FES, desensitization, and sensation focus were applied for 12 weeks [20, 30]. In brief, FES is a technique that uses electrical pulses of low energy to synthetically generate body movements in the individuals who have trouble with their central nervous system (CNS) [31]. At first, the patients were educated about pelvic floor anatomy, while their pelvic floor muscles were massaged by the therapist at each session in the lithotomy position under an infrared light to increase their environmental blood supply. The patients were trained in exercises related to the loosening of pelvic floor muscles and respiratory exercisesso that they could perform them at home. Then, the therapist started to gradually enter one finger into the patient's vagina after obtaining compliance with vaginal examination. If the single finger was well-tolerated by the patient vaginal tampons were prescribed. This action was performed by the patients three times daily at their homes. Again, if tolerated by the patient, vaginal electrodes with tense waves and analgesic frequencies were additionally used for 15 min at each session. At home, the sensation focus technique was performed by the patient's spouse as well. This technique, which includes massaging of the whole body, except for the breasts and genital areas, without vaginal entry, causes the patient to have a feeling of closeness and comfort. Therapeutic meetings continued along with the exercises at home for 12 sessions (1 h each day). Furthermore, the patients' ability to undertake intercourse was assessed based on their reports. In this study, after completing both groups' treatments, the patients' contact numbers and addresses obtained from their medical records were kept so that a trained female interviewer could later complete their questionnaires on basic and demographic information and sexual functioning by visiting them at home. During the study, one of the research members was responsible for managing and providing supervision of the work process and checking some of the questionnaires randomly to detect any empty codes and ensure accuracy of the information. Moreover, one trained expert at the study hospital controlled the completed questionnaires for final accuracy of the information and completed them via follow-up phone calls. Our female sexual function questionnaire contained 19 questions in six domains, including sexual desire, motivation, lubrication, orgasm, sexual satisfaction, and pain. The sexual desire domain included two questions, each with scores 1–5, the total scores of which were then multiplied by 0.6 to achieve the score for the domain. The domains of motivation and lubrication consisted of four questions each, with scores 0–5, the total scores of which were finally multiplied by 0.3 to achieve the score for the domain. Each of the domains orgasm, sexual satisfaction, and pain contained three questions, with scores 0–5, the total scores of which were ultimately multiplied by 0.4 to obtain the scores of each domain.

Sample size

A sample size of 54 women (27 persons in each of the intervention and control groups) was sufficient to detect a clinically significant difference of 25% between the groups in terms of undertaking successful intercourse by using a two-sided Z-

test showing the difference between the proportions with a power of 80% and a significance level of 5%. This difference of 25% represented the difference between a 99.9% response to treatment in the control group and a rate of 75% in the intervention group [20, 32].

All the participants signed written informed consent at the beginning of the study. The research proposal was approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.IKHC.REC.1395.1665).

Statistical analysis

The percentages and mean ± SD values were calculated for the categorical and continuous variables respectively. Chi-squared tests and independent Student's *t* tests were utilized for categorical and continuous variables to evaluate the differences between the two groups of participants respectively. We also used McNemar's test for comparing the proportions of sexual dysfunction in each group and all groups before and after the treatments. A paired *t* test was used to evaluate the mean differences within each of the intervention and standard treatment (control) groups. The utilized assumptions of the parametric statistics conformed to the data by checking the data normality. Multiple analyses of variance (MANOVA) were used to assess the mean differences in scores of the FSFI domains in the intervention and control groups. An inverse probability of censoring weighted (IPCW) log-rank test was employed to compensate for the selection bias caused by censoring (losses) during the study and follow-up periods or for any other reasons in a way that each uncensored subject was inversely weighted by her nonprobability of being censored at the end of her follow-up period [33]. STATA version 13 MP was applied to perform all the statistical analyses, and *p* values of <0.05 were considered to be statistically significant.

Results

In this research, 58 women with lifelong grade III vaginismus and 4 others referred to Imam Khomeini Hospital in Tehran were enrolled. Their mean ages were 30.8 ± 3.9 and 28.8 ± 5.8 years in the intervention and control groups respectively. Table 1 displays a comparison of the insignificantly different demographic information of the two groups of participants at baseline.

Also, in this study, none of the patients in the two groups smoked or had a history of prolapsed pelvic organs or such a condition during examination. Among the total participants, 10 patients (17.2%) had used lidocaine gel, 2 patients (3.4%) had undergone behavior therapy, and 4 patients (7%) had been subjected to hymenectomy before entering the study, but there were no statistically significant differences between the two groups in this respect. The independent *t* test for the variables of age and duration of vaginismus showed no statistically significant differences in the means of the two groups ($p > 0.05$). The results of the nonparametric Chi-squared test for comparing the educational levels of the intervention and control groups showed no significant differences either ($p = 0.24$). Also, 4 (7%), 6 (10.3%), and 2 (3.4%) of the total participants had hypertension, hypothyroidism, and hyperthyroidism respectively. Medical diseases in the two groups revealed no statistically significant differences. Finally, randomization of the subjects into the two groups, intervention and control, led to their comparability at baseline.

Table 1 Baseline characteristics of the studied participants

Baseline characteristics	Intervention group ($n = 30$)	Control group ($n = 28$)
Age (mean ± SD)	30.8 ± 3.9	28.8 ± 5.8
Duration of vaginismus (mean ± SD)	5.11 ± 2.3	3.57 ± 2.11
Gravidity (%)	4(13.33)	3(10.7)
Sexual trauma	2(6.6)	1(3.6)
Psychiatric drug history (%)	2(6.6)	2(7.14)
Constipation (%)	6 (20)	3 (10.7)
Painful intercourse (%)	20 (66.7)	19 (67.9)
Not able to having intercourse (%)	10 (33.3)	9 (32.1)
Educational level (%)		
Secondary	2(6.7)	5(17.9)
Diploma	4(13.3)	6(21.4)
Academic	24 (80)	17(60.7)

Response-to-treatment durations in the intervention and control (physiotherapy) groups were 6.7 ± 3.3 and 8.3 ± 4.3 months respectively, thus showing no statistically significant difference ($P = 0.37$).

The results revealed that the overall prevalence of sexual dysfunction among the studied participants before and after the treatments were 91.4% and 53.4%, respectively. More details are presented in Table 2.

The results shown in Table 2 clearly demonstrate that the frequencies of sexual dysfunction have significantly decreased in the two groups after the treatments, this decrease being higher in the control group.

It was found that 20 out of 30 and 26 out of 28 patients in the intervention and control groups had managed to have successful intercourse respectively. The results of the Chi-squared test showed a significant difference between the two groups in terms of successful intercourse ($p = 0.014$).

The mean differences in the six sexual function domains obtained from the questionnaires before and after the botulinum and physiotherapy treatments using the paired *t* test showed that there were no significant differences within the intervention group in the areas of desire and lubrication compared with the pre-treatments. The results achieved before and after each intervention are listed in Table 3.

Table 2 Within-group comparison of proportion with sexual dysfunction before and after the treatments

Outcome	Category	Before treatment	After treatment	*p* value*
Sexual dysfunction	Intervention group ($n = 30$)	28 (93.3)	20 (66.7)	0.008
	Control group ($n = 28$)	25 (89.3)	11 (39.3)	<0.001
	Total population ($n = 58$)	53 (91.4)	31 (53.4)	<0.001

*McNemar's test

The results shown in Table 3 are indicative of sexual functioning improvements in all six areas in the group treated with physiotherapy. Figure 1 shows the mean differences in each of the six sexual function domains for each treatment group. The graph in Fig. 2 illustrates that the mean scores in the studied areas are significantly higher in the physiotherapy group than in the botulinum group.

Finally, to determine the significant differences between the mean differences of each of the six questionnaire-based sexual functioning domains in the two groups, MANOVA was used. The results in Table 4 show that the use of standard therapy was significantly different from botulinum toxin injections. Also, the results obtained from the IPCW log-rank test were indicative of the non-effectiveness of the non-informative censoring caused by the problems of loss to follow-up on the estimates presented in this study.

Discussion

The findings of this study showed a total of nearly 75% success rates of two the therapeutic methods and significant differences in the treatment outcomes. Evaluation of the efficacies of physiotherapy and botulinum toxin revealed that the standard method of physiotherapy with FES techniques and desensitization had a higher success rate than botulinum toxin injections in all sexual functioning domains and this difference was statistically significant. Also, evaluation of each group before and after treatment demonstrated that lubrication and desire failed to show a significant improvement in the intervention group. Nevertheless, the available evidence was not sufficient for vaginismus treatment based on the applied treatment processes in the selectively treated patients [16]. In recent studies, successful vaginal intercourse has been introduced as the primary outcome of treatment, regardless of the fact that sexual functioning includes six areas that are closely linked with the involved patients' quality of life [34]. In recent years, researchers have concluded that men and women do not respond to sexual problems similarly and have thus introduced the FSFI [29]. In this study, physiotherapy plus electrical stimulation associated with desensitization techniques were assessed against botulinum toxin injections and the results indicated that the standard treatment method was better than the injection approach. In one review study on the effects of botulinum toxin injections, researchers came to the conclusion that this treatment can be a suitable approach to the management of patients suffering from vaginismus [35]. The efficacy of botulinum toxin has been considered a secondary outcome in some other studies using the Lamont criteria and six domains of sexual function, while researchers have concluded its effectiveness even with a single injection [36]. In this study, no increases in the scores of the two areas of lubrication and desire were observed through achieving improved total sexual functioning scores in the patients treated with botulinum toxin.

Table 3 Within-group comparisons of Female Sexual Function Index (FSFI) domains before and after each intervention

	FSFI domains	Mean difference	Standard deviation	*p* value
Physiotherapy group	Desire	1.07	1.39	<0.001
	Arousal	1.96	2.36	<0.001
	Lubrication	2.41	2.0	<0.001
	Orgasm	2.23	1.94	<0.001
	Satisfaction	1.5	1.1	<0.001
	Pain	3.18	2.34	<0.001
Botulinum group	Desire	0.04	0.79	0.79
	Arousal	0.24	0.36	0.008
	Lubrication	0.02	0.11	0.96
	Orgasm	0.82	1.4	0.003
	Satisfaction	0.48	0.6	0.025
	Pain	1.57	1.7	<0.001

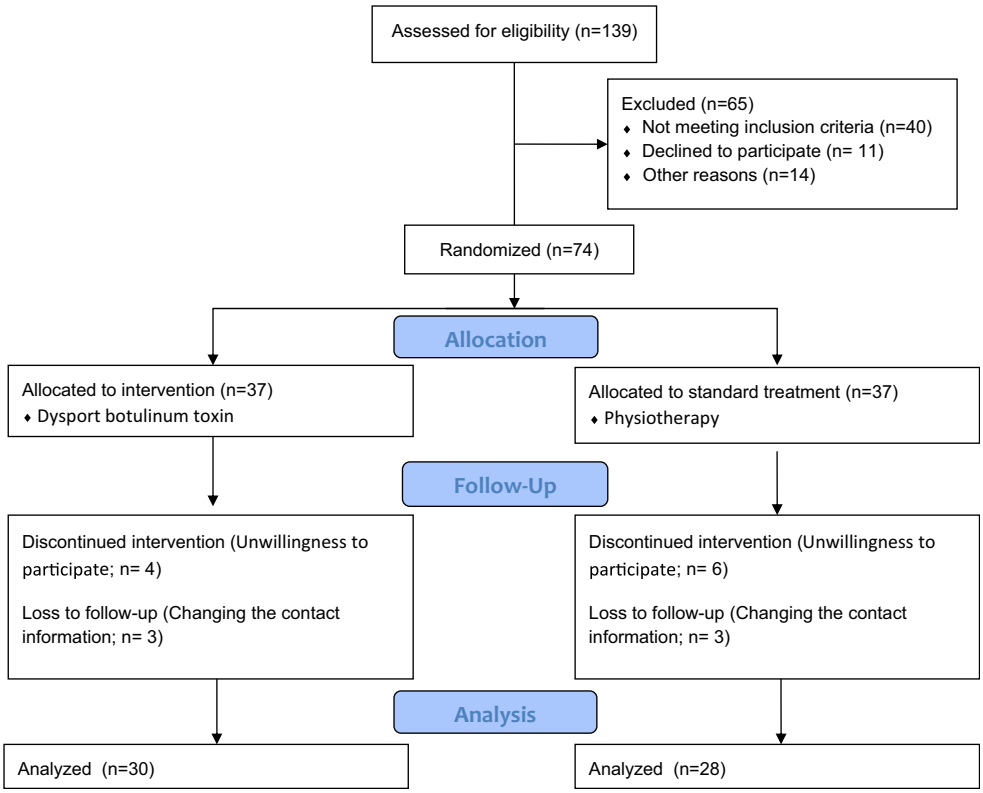

Fig. 1 Study flowchart

Regarding the effectiveness of physiotherapy techniques, this method has been considered first-line treatment in many medical centers, with satisfactory results. A review study examining the effects of physiotherapy on vaginismus has mentioned the positive role of this therapy [23, 37]. In some other serial studies recently conducted on female sexual functioning, the authors confirmed their patients' achievement of pain-free intercourse via a multimodal program aimed at their physical and psychological treatment of vaginismus [38].

The present study further revealed a better sexual functioning index using the mentioned method compared with toxin injection. As referrals to obstetricians and gynecologists are in need of first-line therapies for vaginismus, sufficient education of the involved patients to effectively deal with this condition is of vital importance. Different physical, mental, social, and cultural factors affect the occurrence of vaginismus; thus, it should be considered a multi-dimensional disorder. Most Iranian women do not receive the necessary related education during childhood and adolescence owing to the cultural taboos restricting any education about sexual intercourse and even such beliefs as being sinful or harmful if undertaking it [39]. In addition, the lack of sexual education for men influenced by the above-mentioned stigma and religious rules has decreased their awareness of understanding the difference between sexual desire and sexual cycle among men and women. Perhaps, couples are not given adequate training or patients may refrain from receiving this type of education because of the religious background of Iranian society. Thus, the success rate observed in this study may have been underestimated for the above reasons, especially with regard to the physiotherapy method associated with electrical stimulation techniques. Of course, treatment success rates in Asian countries with the same cultural and religious background were found to be within the same range [40, 41].

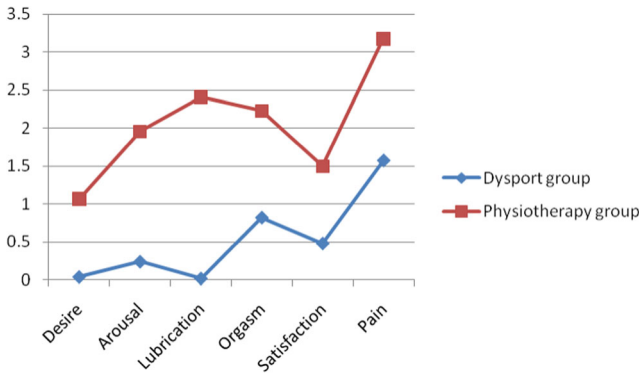

Fig. 2 Mean differences between the intervention and standard treatment groups

Therefore, identification of the primary causes in patients referred for treatment of this disorder is very important. In

Table 4 Between-group comparisons of FSFI domains before and after each intervention using multiple analyses of variance

FSFI domain	Intervention group (mean difference ± SD)	Control group (mean difference ± SD)	F	Mean square	*p* value
Desire	0.04 ± 0.79	1.07 ± 1.39	11.9	15.4	0.001
Arousal	0.24 ± 0.36	1.96 ± 2.36	15.1	42.8	<0.001
Lubrication	0.02 ± 0.11	2.41 ± 2	35.9	84.1	<0.001
Orgasm	0.82 ± 1.4	2.23 ± 1.94	12.2	35.2	0.001
Satisfaction	0.48 ± 0.6	1.5 ± 1.1	12.2	15	0.001
Pain	1.57 ± 1.7	3.18 ± 2.34	8.7	37.6	0.005

cases when the fear of a sexual affair has a psychological origin, another treatment strategy undertaken by a psychiatrist or psychologist may be required [9].

Although the effects of physiotherapy associated with desensitization therapy techniques were compared with those of botulinum toxin injection in this study, acceptably positive results have been achieved by a combination of these methods for treating patients with this disorder in some other studies [42, 43]. It should be said that comparison of the effectiveness of the two mentioned treatments is justified and moral for those who do not have enough time and money to experience both types of treatments. In such cases, doctors can select more appropriate and less aggressive treatments for their patients given the available evidence.

This study considered all the circumstances of the most sensitive phase in a trial, i.e., the participants' random allocation and allocation concealment. Also, considering the large effect sizes reported in other studies, this study with its number of samples seemed to have appropriately sufficient strength to identify the differences investigated by the researchers. It should be mentioned that one of the major problems in clinical studies with several months of follow-up is missing participants during the studies. Unfortunately, a number of eligible participants for the inclusion criteria assigned to the intervention or standard treatment group were excluded from this study for the reasons mentioned in Materials and methods. The inability to provide a comparison of a placebo group as the third arm was one of the limitations of the present research. Nonetheless, the study was conducted in the private setting of the university to investigate the effectiveness of treatments among a population of higher socioeconomic status, in addition to providing a closer relation with the participants.

Treatment with botulinum toxin injection improved the total sexual function index in patients with vaginismus, but could not demonstrate a difference in the areas of desire and lubrication compared with the time before the intervention. Therefore, considering the higher efficacy of standard physiotherapy procedures in accordance with desensitization and electrical stimulation techniques, this treatment method should be regarded as the first-line treatment for vaginismus.

Compliance with ethical standards

Ethical approval All the procedures performed in the human participants studied were in accordance with the ethical standards of the institutional and/or national research committee(s), and with the 1964 Declaration of Helsinki and its later amendments or any other comparable ethical standards.

Informed consent Informed consent was obtained from all the individual participants included in the study.

Conflicts of interest None.

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