

## The effect of botulinum on chronic pelvic pain and sexual satisfaction in endometriosis

Fatemeh Davari Tanha <sup>a</sup>; Mojgan Asadi <sup>b,c\*</sup>; Faeze Mirbagheri <sup>d</sup>; Elham Feizabad <sup>d</sup>; Zahra kaveh<sup>e</sup> Kazem Mousavizadeh <sup>f</sup>

### Abstract

**Background and Objective:** Endometriosis is a chronic gynecological condition that affects approximately 10% of women of reproductive age. Chronic pelvic pain is a common symptom of endometriosis and can have a significant impact on a woman's quality of life, including sexual satisfaction. Botulinum toxin injection has been used as a treatment for chronic pelvic pain in endometriosis, but its effect on sexual satisfaction is not well understood.

**Methods:** A randomized controlled trial was conducted to evaluate the effect of botulinum toxin injection on chronic pelvic pain and sexual satisfaction in women with endometriosis. The study included 32 women with endometriosis who were randomly assigned to receive either botulinum toxin injection or placebo. The primary outcome measure was change in chronic pelvic pain assessed using the visual analog scale (VAS) at one month after treatment. Secondary outcome measures included changes in sexual satisfaction assessed using the Female Sexual Function Index (FSFI) at one month after treatment.

**Results:** The results showed that botulinum toxin injection significantly reduced chronic pelvic pain compared to placebo at one month after treatment ( $p < 0.001$ ). There was also a significant improvement in sexual satisfaction in the botulinum toxin group compared to placebo at one month after treatment ( $p = 0.001$ ).

**Conclusion:** Botulinum toxin injection may be an effective treatment option for women with endometriosis, chronic pelvic pain and sexual dysfunction.

This research was also registered with the code IRCT20091012002576N20 in the Clinical Trial Registration Center of Iran.

Keywords: botulinum, chronic pelvic pain, endometriosis, sexual satisfaction

**Introduction:**

Chronic pelvic pain is a common condition that affects many women worldwide. It is characterized by persistent pain in the lower abdomen, pelvis, and genital area that lasts for more than six months.(1) Endometriosis is one of the leading causes of chronic pelvic pain in women. It is a condition where the tissue that normally lines the uterus grows outside of it, causing inflammation and scarring (2-5).

Endometriosis can have a significant impact on a woman's sexual health and satisfaction. The pain associated with the condition can make sexual intercourse uncomfortable or even unbearable. This can lead to decreased sexual desire and satisfaction, which can have negative effects on a woman's overall quality of life.(6) Botulinum toxin is a neurotoxin that works by blocking nerve signals to muscles, reducing muscle contractions and spasms. Botulinum toxin injection has been found to be an effective treatment for chronic pelvic pain and sexual dysfunction in conditions other than endometriosis. In a study conducted on women with vulvodynia, botulinum toxin injection was found to significantly reduce pain and improve sexual satisfaction.(7) The other studies showed that the injection of botulinum toxin into the pelvic floor muscles reduced muscle tension and spasms, which are often associated with chronic pelvic pain.(8, 9)

So, botulinum toxin injection has been proposed as a potential treatment for these symptoms, but there is limited research on its effectiveness in endometriosis. Therefore, designing a study that uses botulinum toxin injection on chronic pelvic pain and sexual satisfaction in endometriosis was necessary to determine its efficacy. The study provided valuable insights into the use of botulinum toxin injection as a treatment option for endometriosis-related symptoms. It will help clinicians make informed decisions about whether to recommend this treatment to their patients. Additionally, the study will contribute to the growing body of research on endometriosis and its management, which can lead to improved patient outcomes. Furthermore, designing a study that uses botulinum toxin injection on chronic pelvic pain and sexual satisfaction in endometriosis will help identify any potential side effects or risks associated with this treatment. This information is crucial for patient safety and informed consent. By understanding the risks and benefits of botulinum toxin injection, patients can make informed decisions about their treatment options and feel more empowered in managing their condition..

**Material and Methods:**

A randomized controlled trial was conducted to evaluate the effect of botulinum toxin injection on chronic pelvic pain and sexual satisfaction in women with endometriosis between July 2021 and July 2022 at a tertiary care university hospital (Yas Hospital Complex).

The study included 32 women with endometriosis who were randomly assigned to receive either botulinum toxin injection or placebo. The sample size for each group was calculated to be 16, using the clinical trial superiority design formula and the reported values in the previous study, the study power of 80%, and the two-tailed significance level of 5% (10). The inclusion criteria for the patient group were age between 18 and 50, history of endometriosis at surgery, Persistent pelvic pain for at least 6 months and pelvic floor spasm. The exclusion criteria were other causes of chronic pelvic pain including gastrointestinal, psychological disorders, infectious, fibromyalgia and chronic fatigue syndrome, untreated severe cervical dysplasia, history hysterectomy and bilateral salpingo-oophorectomy, allergy to botulinum toxin, history of myasthenia gravis or Eaton-Lambert syndrome, history of urinary or fecal incontinence, pelvic prolapse, Pregnancy, Lactation. Menopausal people were excluded from the study, and patients did not receive hormonal drugs for at least two months before the study.

The primary outcome measure was change in chronic pelvic pain assessed using the visual analog scale (VAS) at one month after treatment. Secondary outcome measures included changes in sexual satisfaction assessed using the Female Sexual Function Index (FSFI) at one month after treatment. All participants underwent vaginal sonography or laparoscopy for diagnosis and staging of endometriosis before enrollment in the study (11). Participants were excluded if they had any contraindications to botulinum toxin injection or if they had undergone previous surgery for endometriosis within the past 6 months. First, muscle spasm and pain in the pelvic region were evaluated by vaginal finger examination in eligible people to participate in the study, and the presence and location of the spasm was recorded. Then, after randomization by block randomization method, people were placed in botulinum injection group (intervention group) and control group (saline injection). The injection method is as follows: the women were placed in the lithotomy position, after that single digit palpation was used to assess the presence of muscle spasm in the pelvic floor muscles. After the examination and 20 to 30 minutes before the injection, up to 10 mg of diazepam was administered orally, and 4% lidocaine cream was applied to the spasm site in the vaginal mucosa. In the intervention

group, a vial of 100 units of Anabotulinum toxin A (Botox) was placed in 4 ml of saline (final concentration of 25units/ml). A total of 100 units of botulinum are injected into the spasmodic muscles. The injections are made using a 27-gauge needle. The injections are placed at a depth of 5-10 mm. The injection was performed by a gynecologist with experience in the field of endometriosis using a sterile technique. In fact, a total dose of 100 units was divided among three to four marked areas of muscle spasm. The authors of the article noted that the injection method was well-tolerated by the women in the study. Bilateral injections in muscles including pubococcygeus, iliococcygeus and internal obtrator were performed through transvaginal. Participants were followed up at one month after treatment.

### **Results:**

The first step, we identified potential participants who meet the eligibility criteria, which may include age, diagnosis of endometriosis, and chronic pelvic pain. Once eligible participants have been identified, they are randomly assigned to either the treatment group or the control group. The injections are administered by gynecologist and participants are monitored for any adverse effects. Fallow-up visit are scheduled at 4week to assess changes in chronic pelvic pain and sexual satisfaction over time. The data collected during the visit is analyzed to determine if there is a significant difference between the treatment and control groups. (figure1)

The demographic characteristics of the studied population are shown in table 1. The results showed that botulinum toxin injection significantly reduced chronic pelvic pain compared to placebo at one month after treatment ( $p<0.001$ ). The average sedative drug usages in intervention group were lower with no significant difference between the two groups ( $P=0.12$ ). (table2) There was also a significant improvement in sexual satisfaction in the botulinum toxin group compared to placebo at one month after treatment ( $p=0.001$ ) (table3). The comparison of sexual satisfaction after the intervention between the case and control groups showed that the components of satisfaction ( $P<0.001$ ), dyspareunia ( $P<0.001$ ), orgasm ( $P=0.001$ ) were significantly better in the case group than the control group. However, there was no statistically significant difference between the two groups regarding the score of libido ( $P=0.32$ ), psychological stimulation ( $P=0.09$ ), wetness ( $P=0.11$ ). (table4) In general, the total score of sexual satisfaction after the intervention showed a statistically significant difference between the two groups. No side effects caused by botulinum injection (urinary retention, constipation, urinary and fecal incontinence, back pain, etc.) were reported in this study.

**Discussion:**

Chronic pelvic pain is a common symptom of endometriosis, a condition where the tissue that normally lines the inside of the uterus grows outside of it. This can cause pain and discomfort during menstruation, sexual intercourse, and other activities. Sexual satisfaction can also be affected by endometriosis due to pain during intercourse and decreased libido.(12-14) Botulinum toxin injection has been used as a treatment for chronic pelvic pain in conditions other than endometriosis. It works by blocking the release of acetylcholine, a neurotransmitter that causes muscle contractions.(15) This can help reduce pain and improve sexual function. On one hand, some studies have shown that botulinum toxin injection can provide relief from chronic pelvic pain in other than endometriosis. In these studies, women who received botulinum toxin injection reported a 50% reduction in pain compared to those who received a placebo injection (16, 17) Tandon HK et al investigated the effect of botulinum toxin injection on chronic pelvic pain in women with endometriosis. The case series included 13 women who received botulinum toxin injections into their pelvic floor muscles. The results showed that the treatment significantly improved muscle spasms and pelvic pain at 4-8 weeks post-treatment.(16) Stratton et al evaluated the efficacy of botulinum toxin injection in women with endometriosis-associated chronic pelvic pain. The study included 30 women who received botulinum toxin injections into their pelvic floor muscles. The results showed that the treatment significantly reduced pain scores one month post-treatment.(17)

A systematic review analyzed data from 5 randomized controlled trials and 12 observational studies that investigated the effect of botulinum toxin injection on chronic pelvic pain. All observational studies of the review found that botulinum toxin injection was effective in reducing chronic pelvic pain with the greatest change in visual analog scale from 8.69 at baseline to 3.07 at 24 months post-injection. However, only one of the five randomized controlled trials found that women who received botulinum toxin injection had improved chronic pelvic pain compared to those who did not receive the treatment.(18)

On the other hand, some of studies do not support the use of this treatment method. One study conducted by Petersen et al investigated the effect of Injection of 20 I.E. Botox in the vestibule

of women diagnosed with vestibulodynia. Botox does not reduce pain, improve sexual functioning, or impact the quality of life compared to placebo. (19)Yaraghi et al compared the effectiveness functional electrical stimulation of pelvic floor muscles for treating sexual dysfunction with botulinum treatment. The study found that physiotherapy procedure was more effective than botulinum treatment.(20)

In comparison, our study focused on the use of botulinum toxin injection as a potential treatment option for endometriosis- related chronic pelvic pain and sexual satisfaction. Our findings suggest that botulinum toxin injection can significantly reduce chronic pelvic pain and improve sexual satisfaction in these patients. In this study, we found that women who received botulinum toxin injections had significantly lower levels of pain during intercourse compared to those who did not receive the injections. In our study compared sexual satisfaction in women with endometriosis who received botulinum toxin injections versus those who did not. The study found that women who received botulinum toxin injections had significantly higher levels of sexual satisfaction compared to those who did not receive the injections. This suggests that botulinum toxin injections may be an effective treatment option for improving sexual function in women with endometriosis.

However, there are also some potential side effects of botulinum toxin injection, such as urinary retention and constipation.(21) These side effects can affect quality of life and may need to be managed with additional treatments.

It is important to note that botulinum toxin injection is not a cure for endometriosis. It only provides temporary relief from symptoms such as chronic pelvic pain and painful intercourse. (22)Women with endometriosis should work closely with their healthcare provider to develop an individualized treatment plan that addresses their specific needs.

Overall, our study provides valuable insight into the potential benefits of botulinum toxin injection for endometriosis patients suffering from chronic pelvic pain and sexual dysfunction. However further research is needed to fully understand the long-term effects of this treatment option. It is important to weigh the potential benefits against the risks and side effects before deciding on this treatment option. Other treatments such as hormonal therapy or surgery may also be considered depending on individual circumstances.

**Conclusion:** chronic pelvic pain associated with endometriosis can have a significant impact on a woman's sexual health and satisfaction. Botulinum toxin injection may be an effective

treatment option for reducing pain during intercourse and improving sexual function in women with endometriosis. However, further research is needed to fully understand the long-term effects of this treatment option on sexual health and overall quality of life for women with endometriosis.

### **Statements & Declarations:**

#### **Funding:**

No funding was obtained.

#### **Conflict of Interest:**

The authors declare no conflict of interest.

#### **Author's Contributions**

Fatemeh Davari Tanha conceived and designed the study ;Mojgn Asadi designed the study and wrote paper; Faeze Mirbagheri collected the data; Elham Feizabad performed the analysis; Zahra kaveh edited the paper and Kazem Mousavizadeh developed project.

#### **Acknowledgment:**

The authors would like to express their gratitude to all participants enrolled in this project.

#### **Ethics approval:**

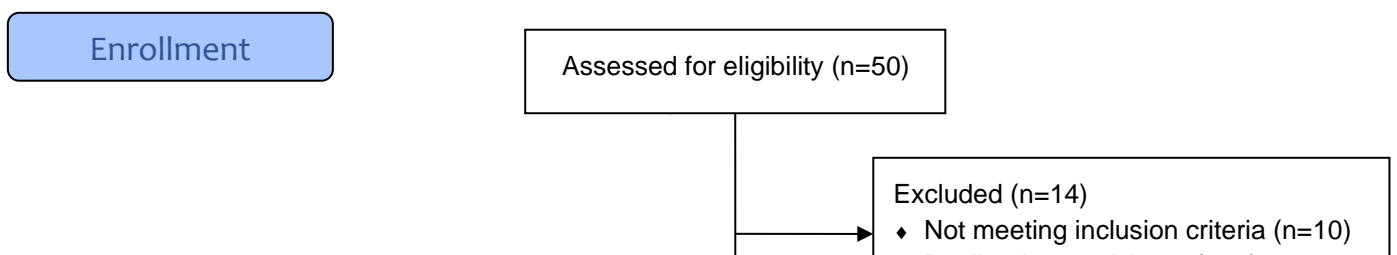
The study was approved by the Research Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.MEDICINE.REC.1400.258).

#### **Consent to participate:**

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

### **Figure 1**

**Consort diagram showing the sequence of enrollment, allocation, follow-up, data analysis**



Article in Press

Table 1: Demographic characteristic of studied population

Demographic characteristic	Group	Mean	Std. Deviation	P-value
Age	control	37.38	6.70	0.897
	case	36.94	5.26	



BMI	control	25.34	5.08	1.000
	case	24.44	4.00	
Chronic pelvic pain	control	7.13	1.45	0.056
	case	8.06	1.12	
Dysmenorrhea	control	2.81	1.04	0.051
	case	2.25	0.93	

Table 2 comparison of pain components in case and control groups

Pain component	Group	Mean	Std. Deviation	P-value
----------------	-------	------	----------------	---------

Chronic pelvic pain	control	3.37	0.62	0.001
	case	2.25	0.93	
dysmenorrhea	control	2.81	1.04	0.051
	case	2.25	0.93	
Daily need for pain medication	control	1.18	0.83	0.128
	case	0.68	0.60	

Table 3 comparison of pain components in control group before and after intervention

Case Group	Mean	Std. Deviation	P-value
------------	------	----------------	---------

Chronic pelvic pain before intervention	8.06	1.12	<0.001
Chronic pelvic pain after intervention	2.25	0.93	
Dysmenorrhea before intervention	7.50	1.51	<0.001
Dysmenorrhea after intervention	2.25	0.93	
Daily need for pain medication before intervention	3.88	1.20	<0.001
Daily need for pain medication after intervention	0.69	0.60	

Table 4 comparison of female sexual function index in two groups of case and control

FSFI domain	Group	Mean	Std. Deviation	P-value
-------------	-------	------	----------------	---------

Desire	control	4.09	0.39	0.323
	case	4.28	0.48	
arousal	control	4.05	0.31	0.094
	case	4.22	0.35	
lubrication	control	3.90	0.41	0.110
	case	3.90	0.41	
orgasm	control	4.13	0.38	0.003
	case	3.70	0.34	
satisfaction	control	4.03	0.47	<0.001
	case	4.70	0.31	
pain	control	3.70	0.18	<0.001
	case	1.75	0.29	
Total score	control	23.89	1.01	0.001
	case	23.89	1.01	

## References:

1. MEDVEDEVA L, ZAGORULKO O, SHEVTSOVA G. Botulinum toxin treatment of neuropathic pain. *Russian Journal of Pain*. 2020;18(2):34-9.
2. Dayal S. Ovarian endometriosis with borderline serous tumor-Association or coincidence– A case report and review of literature. *Indian Journal of Medical and Paediatric Oncology*. 2020;41(03):406-8.
3. Laschke MW, Menger MD. Basic mechanisms of vascularization in endometriosis and their clinical implications. *Human reproduction update*. 2018;24(2):207-24.
4. McKinnon BD, Bertschi D, Bersinger NA, Mueller MD. Inflammation and nerve fiber interaction in endometriotic pain. *Trends in Endocrinology & Metabolism*. 2015;26(1):1-10.
5. Sampson JA. Peritoneal endometriosis due to menstrual dissemination of endometrial tissue into the peritoneal cavity. *Am J Obstet Gynecol*. 1927;14:422-69.
6. Pluchino N, Wenger J-M, Petignat P, Tal R, Bolmont M, Taylor HS, et al. Sexual function in endometriosis patients and their partners: effect of the disease and consequences of treatment. *Human reproduction update*. 2016;22(6):762-74.
7. Karp BI, Tandon H, Vigil D, Stratton P. Methodological approaches to botulinum toxin for the treatment of chronic pelvic pain, vaginismus, and vulvar pain disorders. *International urogynecology journal*. 2019;30:1071-81.
8. Morrissey D, El-Khawand D, Ginzburg N, Wehbe S, O'Hare III P, Whitmore K. Botulinum toxin A injections into pelvic floor muscles under electromyographic guidance for women with refractory high-tone pelvic floor dysfunction: a 6-month prospective pilot study. *Urogynecology*. 2015;21(5):277-82.
9. Abbott JA, Jarvis SK, Lyons SD, Thomson A, Vancaille TG. Botulinum toxin type A for chronic pain and pelvic floor spasm in women: a randomized controlled trial. *Obstetrics & Gynecology*. 2006;108(4):915-23.
10. Naumann M, So Y, Argoff C, Childers M, Dykstra D, Gronseth G, et al. Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Assessment: botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2008;70(May 6 (19)):1707-14.
11. Moradi B, Gity M, Davari Tanha F, Golestani Jahromi M, Fayyazi S. Evaluation of the Diagnostic Value of TVS (Transvaginal sonography) in the Diagnosis of Pelvic Endometriosis in Comparison with Laparoscopic Evaluation in Patients Referred to the Imaging Center of Imam Khomeini Hospital and Yas Hospital of Tehran in 2018. *Journal of Obstetrics, Gynecology and Cancer Research*. 2022;7(4):272-8.
12. Falcone T, Lebovic DI. Clinical management of endometriosis. *Obstetrics & Gynecology*. 2011;118(3):691-705.
13. Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. *Journal of assisted reproduction and genetics*. 2010;27:441-7.
14. Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. *Best practice & research Clinical obstetrics & gynaecology*. 2004;18(2):177-200.
15. Iversen L. Substance P equals pain substance? *Nature*. 1998;392(6674):334-5.

16. Tandon HK, Stratton P, Sinaii N, Shah J, Karp BI. Botulinum toxin for chronic pelvic pain in women with endometriosis: a cohort study of a pain-focused treatment. *Regional Anesthesia & Pain Medicine*. 2019;44(9):886-92.
17. Stratton P, Tandon HK, Phan V, Aredo JV, Sinaii N, Shah J, et al. Randomized, placebo-controlled trial of botulinum toxin for endometriosis-related chronic pelvic pain. *Fertility and Sterility*. 2021;116(3):e52.
18. Luo FY, Nasr-Esfahani M, Jarrell J, Robert M. Botulinum toxin injection for chronic pelvic pain: A systematic review. *Acta Obstetrica et Gynecologica Scandinavica*. 2020;99(12):1595-602.
19. Petersen CD, Giraldi A, Lundvall L, Kristensen E. Botulinum toxin type A—a novel treatment for provoked vestibulodynia? Results from a randomized, placebo controlled, double blinded study. *The journal of sexual medicine*. 2009;6(9):2523-37.
20. Yaraghi M, Ghazizadeh S, Mohammadi F, Ashtiani EM, Bakhtiyari M, Mareshi SM, et al. 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. *International urogynecology journal*. 2019;30:1821-8.
21. Adelowo A, Hacker M, Shapiro A. Botulinum toxin type A (BOTOX) for refractory myofascial pelvic pain. *Female Pelvic Med Reconstr Surg*. 2013; 19: 288–92. Study showing the efficacy of botulinum toxin in MPS of pelvic floor.
22. Rubin R. Botulinum toxin to treat endometriosis pain. *JAMA*. 2019;322(8):716-.