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Original Research

A Novel, Non-opioid Treatment for Chronic Pelvic Pain in Women with Previously Treated Endometriosis Utilizing Pelvic-Floor Musculature Trigger-Point Injections and Peripheral Nerve Hydrodissection

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Abstract

Background: Endometriosis is the abnormal growth of uterine tissue outside the uterine cavity that can cause chronic pain, dysmenorrhea, and dyspareunia. Although the disease is common and nonmalignant in nature, the symptoms can severely impact function and quality of life. Treatment options for endometriosis are limited and not well understood despite a growing need.
Objective: To determine the effectiveness of pelvic-floor musculature trigger-point injections and peripheral nerve hydrodissection in treating endometriosis symptoms, associated pain, and pelvic functionality.
Design: Retrospective longitudinal study case series.
Setting: Private practice.
Patients: Sixteen female patients with biopsy-confirmed endometriosis.
Interventions: Ultrasound-guided pelvic-floor trigger-point injections and peripheral nerve hydrodissection performed once a week for 6 weeks.
Main Outcome Measurements: Pelvic pain intensity as measured pretreatment and posttreatment by the 0 to 10 Visual Analogue Scale (VAS) and the Functional Pelvic Pain Scale (FPPS).
Results: Pretreatment, the mean VAS score was 6.0 (standard deviation [SD] 2.7), and posttreatment the mean VAS score was 2.9 (SD 2.6); $P < .05$, 95% confidence interval (CI) 1.16 to 4.97. The mean total FPPS score before treatment was 14.4 (SD 5.2) and posttreatment it was 9.1 (SD 5.8); $P < .05$, 95% CI 1.34 to 9.28. Analysis of the subcategories within the FPPS indicated that the improvement was statistically significant in the categories of intercourse, sleeping, and working. In the category of intercourse, the mean change in score after treatment was 1.3 ($P < .05$, 95% CI 0.26-2.31). In the category of sleeping, the mean change in score after treatment was 1.2 ($P < .05$, 95% CI 0.32-1.99). In the category of working, the mean change in score after treatment was 0.9 ($P < .05$, 95% CI 0.18-1.53).
Conclusions: Analysis suggests that the treatment was effective at relieving pain related to endometriosis; it also reflected promise in improving overall pelvic function, particularly in relation to intercourse, working, and sleeping.
Level of Evidence: IV

Introduction

Endometriosis is characterized by the abnormal growth of uterine tissue outside the uterine cavity, primarily on the pelvic peritoneum, ovaries, and rectovaginal septum.[1] Women with endometriosis typically present with dysmenorrhea, pelvic pain, lower abdominal pain, abdominal bloating, dyspareunia, constipation, and painful defecation, and some patients have urinary symptoms such as urgency, frequency, and burning with urination. Symptoms are known to be painful and debilitating to patient function, affecting sleep, employment, sexual function, and mood. Women with endometriosis related to dyspareunia have lower sexual function, which decreases their quality of life and causes

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relationship distress with their partners.[2] Endometriosis affects approximately 5% of women of reproductive age, particularly between 25 and 35 years of age.[3] The estimated total annual cost of surgically confirmed endometriosis is $1.8 million.[4] Chronic pelvic pain (CPP) resulting from endometriosis is multifactorial, with neuropathic, myofascial, and central pain components.[5]

Endometriosis resulting in neuropathic pain may occur due to invasion of endometriosis into pelvic nerves or spontaneous pain resulting from compression of pelvic nerves including the obturator, pudendal, ilioinguinal, iliohypogastric, genitofemoral, or lateral femoral cutaneous nerve.[6] The sensory fibers innervating endometrial lesions include C-fiber nociceptors, which respond to noxious stimuli in the periphery including immune and inflammatory factors.[7] Multiple factors are prevalent in endometriosis, including tumor necrosis factors-α; interleukin (IL)-1, IL-6, IL-8, and IL-10; and prostaglandins E2 and F, which directly or indirectly activate nociceptors.[8] Peripheral sensitization occurs as a result of the lowered activation threshold of nociceptors due to their prolonged or recurrent activation.[9] Nociceptors can facilitate sensitization by secreting neuropeptides, which initiate neurogenic inflammation, increasing receptor expression along peripheral terminals, and activating previously inactive visceral nociceptors with intense stimulation.[10-13] Continuous nociceptor activation sends afferent signals to the spinal cord, which cause structural and functional changes, ultimately leading to central sensitization and an exaggerated response to peripheral stimuli.[14] Clinically, central sensitization results in allodynia, hyperalgesia, and referred pain. Often, patients with CPP seek treatment from various health care providers without finding a definitive diagnosis or treatment plan. Recognizing central sensitization in CPP can help the physician and the patient to understand the physiology behind their symptoms and offer management strategies to defeat the cycle.

Myofascial dysfunction and associated trigger points contribute to CPP and have been associated with endometriosis.[15,16] The muscles of the pelvic floor are arranged in two main layers: the superficial layer and the deep layer. The superficial layer, which is part of the urogenital diaphragm, is composed of the bulbospongiosus, ischiocavernosus, and superficial and deep transverse perineal muscles. The deep layer forms the pelvic diaphragm and is known as the levator ani muscle group, consisting of the puborectalis, pubococcygeus, and the iliococcygeus. These muscles and their associated innervations can be seen in Figure 1. Other deep muscles include the external rotators of the hip: piriformis, quadratus femoris, superior and inferior gamelli, and the obturator internus. A recent study attributed pelvic myofascial dysfunction or trigger points as the source of pain in 13.2% of screened patients with CPP, with an even higher prevalence of patients with pelvic floor muscle tenderness.[17] In another study, nearly 1000 women with CPP were screened and 22% were noted to have pain with palpation of the levator ani muscles.[18] In addition, one final study compared clinically detectable pelvic floor muscle tenderness in healthy women volunteers and women with CPP, and found it was significantly higher in the latter group, 58.3% compared to 4.2%.[19]

With CPP, there is cross-sensitization among the structures of the pelvis including the uterus, bladder, and colon, and their surrounding supporting structures, as well as the pelvic floor musculature itself.[20] Cross-sensitization in these pelvic structures means noxious stimuli from the affected structure is transmitted to an adjacent normal structure, causing functional changes in the latter. This occurs via convergent neural pathways of the noxious stimulus transmission from two or more organs. In other words, sensory information from individual structures converge at shared sensory neural pathways throughout the central nervous system (CNS), including at the dorsal root ganglion, the spinal cord, and the brain. This viscerosomatic convergence explains how the ongoing noxious visceral input can sensitize multiple areas of the spinal cord, generating the broad areas of allodynia, hyperalgesia, and referred pain seen with somatic dysfunction.[20]

Treatment options for endometriosis-related symptoms are not well understood despite a rising need. Traditionally, treatments for endometriosis have focused on hormonal therapies and excision surgery, both of which target ectopic endometrial lesions. These approaches are essential in excising and decreasing the extent and recurrence of the pro-inflammatory endometriosis lesions.[21] However, pain often persists following hormonal treatments and excision surgeries due to myofascial pain, neurogenic inflammation and central sensitization. Other treatment modalities for CPP related to endometriosis include neural blockade, decompressive and surgical interventions, medical management, physical therapy, and alternative modalities.[6] Nerve blocks are both diagnostic and therapeutic. Practitioners may use diagnostic nerve blocks to easily accessible peripheral nerves such as ilioinguinal or lateral femoral cutaneous nerves to confirm diagnosis.[22,23] Nerve blocks are used to reduce spontaneous ectopic activity of the involved nerve in many peripheral neuropathic pain disorders. Arner et al conducted a study on 38 patients with bupivacaine block injections where 18 patients experienced prolonged relief that exceeded 12 hours.[24] Published trials of gabapentin and tricyclic antidepressants for both generalized pelvic pain and for vulvar pain show conflicting results.[25,26] In addition, although many women may self-medicate with nonsteroidal antiinflammatory medications over the counter, evidence on their efficacy is lacking.[27] For neuropathic pain, topical local anesthetics and topical capsaicin may be effective in treating localized pain and can be used as an adjunctive treatment, but they do not encompass the complete process involved in endometriosis-associated pelvic pain.[28,29] Trigger point injections with local

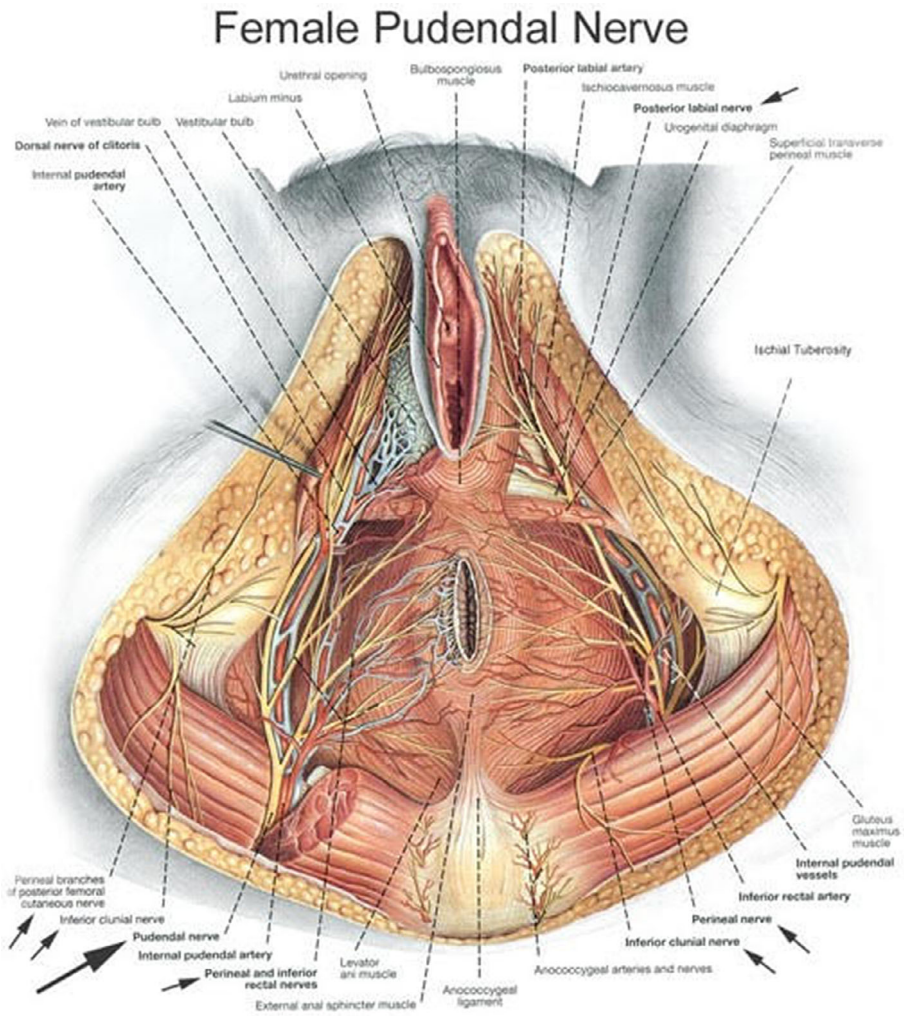

Figure 1. The levator ani are made up of the iliococcygeus, pubococcygeus, and puborectalis muscles. The female pudendal nerve innervates the levator ani. (Paulsen, Waschke, Sobotta Atlas of Human Anatomy, 16th Edition 2018 Elsevier GmbH, Urban & Fischer, Munich.)

anesthetics, such as lidocaine or bupivacaine, with or without corticosteroids, have been utilized to treat myofascial pain conditions associated with CPP.[5] Peripheral nerve hydrodissection involves using an anesthetic or solution to separate the nerve from surrounding tissue, fascia, and adjacent structures, allowing the nerves to reset and decrease hypersensitivity.[30]

The objective of this study is to determine the effectiveness of external, ultrasound-guided pelvic floor musculature trigger-point injections combined with peripheral nerve hydrodissection in treating endometriosis-related symptoms caused by the triad of myofascial pain, peripheral neurogenic inflammation, and central sensitization.

Methods

Participants

Participants were 16 female patients between the ages of 21 and 67 years old who presented to an outpatient pelvic rehabilitation private practice with a diagnosis of endometriosis via positive pathology from intraoperative biopsy and CPP. Patient demographics can be seen in Table 1. All participants underwent pretreatment evaluations with a detailed history and physical examination, including an internal pelvic floor examination performed by one of three physiatrists. This consisted of examination of the levator ani musculature sling, including strength, muscle tone, and tenderness to palpation to diagnose trigger points, defined as palpable taut bands with a referred pain pattern. Commonly referred pain patterns include lower abdomen, medial thigh, buttocks, and perineum. In addition, the pudendal nerve was assessed with palpation over Alcock canal and the ischial spines to check for tenderness or a tingling sensation known as Tinel's sign. The inclusion criteria included a history of endometriosis (confirmed by pathology), history of pelvic pain greater than 6 months duration, and completion of at least 3 months of pelvic floor physical therapy. The exclusion criteria included failure to complete a 3-month course of pelvic floor physical therapy prior to treatment protocol, malignancy, and active pregnancy.

Table 1
Patient characteristics including age, duration of pelvic pain, relevant past medical and surgical history, medications for pain control, and current hormonal treatments

Patient #	Age	Duration of pelvic pain (years)	Past gynecological medical history	Past surgical history (# times)	Medications	Hormonal treatments
1	21	1.5	None	Endometriosis surgery (1)	Diazepam suppository, amitriptyline, and hydroxyzine	None
2	22	11	None	Endometriosis surgery (2)	Acetaminophen #3, sertraline, clonazepam, PO diazepam, diazepam suppository, and zolpidem tartrate	Birth control pill
3	23	12	None	Endometriosis surgery (4)	CBD Tabs, duloxetine, BC pill, and hydroxyzine, milnacipran HCl, pregabalin, and topical ketamine HCl cream to lower abdomen and sacrum	Birth control pill
4	23	10	Vulvodynia, Fibromyalgia	Endometriosis surgery (1)	Sertraline, ketamine HCl cream, CBD suppository, gabapentin, duloxetine, and hydroxyzine	Birth control pill
5	24	9	None	Endometriosis surgery (2)	Gabapentin, amitriptyline, meloxicam, acetaminophen, and pregabalin	None
6	25	15	Adenomyosis, Interstitial Cystitis	Endometriosis surgery (3)	Diazepam suppository, Diclofenac, duloxetine	Birth control pill
7	27	16	Interstitial Cystitis	Endometriosis surgery (1)	Diazepam suppository, diclofenac	Birth control pill
8	27	13	Ovarian Cysts Rupture	Endometriosis surgery (2)	Diazepam suppository, NSAIDs, hydroxyzine	Birth control pill
9	29	10	None	Endometriosis surgery (1)	Diclofenac, amitriptyline, diazepam suppository, methocarbamol, hydroxyzine	Birth control pill
10	29	17	Ovarian Cysts	Endometriosis surgery (5)	Oxycodone/acetaminophen 10/325, diclofenac, duloxetine, ketamine HCl cream	Mirena IUD
11	36	5	None	Endometriosis surgery (5), Hysterectomy	Iibuprofen PRN, escitalopram, milnacipran HCl, diazepam suppository	Birth control pill, Mirena IUD
12	36	18	None	Endometriosis surgery (2)	Venlafaxine, diazepam suppository, rizatriptan, pregabalin,	Birth control pill
13	38	14	Recurrent UTIs	Endometriosis surgery (2)	Milnacipran HCl, ibuprofen, diazepam suppository	Birth control pill
14	43	33	Adenomyosis	Endometriosis surgery (2)	Diazepam Suppository, Milnacipran HCl, ibuprofen	None
15	48	18	Interstitial Cystitis, Ovarian Cysts	Endometriosis surgery (1)	Diazepam suppository, oxycodone/acetaminophen, CBD suppository	Lupron
16	67	29	Ovarian Cancer	Endometrial resection (1)	Gabapentin, CBD tabs and oil, acetaminophen, sertraline, milnacipran HCl, pregabalin, medical marijuana	None

Procedures

A retrospective chart review was done upon institutional review board (IRB) approval (IRB# 17-0761). The medical director developed the treatment protocol for patients who failed to progress with physical therapy alone using the theories behind the generators of CPP and previously successful treatments.[5,17,24,30] The protocol consisted of external ultrasound guided pelvic-floor trigger-point injections to the bilateral iliococcygeus, pubococcygeus, and puborectalis musculature, as all three muscles are involved in CPP. Each muscle was treated one time for a total of six injections over 6 weeks. Patients were placed in the prone position using a subgluteal posterior approach, and a flexible 6- inch, 27-gauge needle was used to place 2 mL of 1% lidocaine in each muscle. Patients concurrently underwent ultrasound-guided peripheral nerve hydrodissection performed on the pudendal nerve as well as the posterior femoral cutaneous nerve, alternating right and left sides throughout the protocol. For the first treatment on each side 2 mL of dexamethasone with 5 mL of 1% lidocaine was placed around each nerve. Dexamethasone was used initially to reduce neurogenic inflammation due to an onset of action within 72 hours. For the subsequent treatments, 2 mL of Traumeel with 5 mL of 1% lidocaine was used for peripheral nerve hydrodissection. Traumeel is a homeopathic, plant derived anti-inflammatory medication consisting of 14 diluted

biologic and mineral components including *Echinacea angustifolia, Arnica montana*, and *Hypericum perforatum* (St John's wort).[31] In a study by Porozov et al, Traumeel was found to inhibit IL-1 β and TNF-α secretion resulting in its anti-inflammatory effects. Traumeel has shown efficacy comparable to nonsteroidal anti-inflammatory drugs (NSAIDs) in terms of decreasing inflammation and accelerating recovery in patients with pain and swelling associated with musculoskeletal injuries.[32] As a result, Traumeel was used in this study for subsequent treatments to decrease inflammation and reduce the need for further steroid use. These treatments were performed once a week for 6 weeks and were all office-based procedures without anesthesia.

In addition, each patient was involved in an individualized pelvic-floor physical therapy program before and during the treatment process. The pelvic-floor physical therapy included both internal and external myofascial release of the pelvic-floor musculature, scar tissue mobilization, visceral mobilization, skin rolling along lower abdomen and buttocks, nerve gliding along the pudendal nerve and its branches, the posterior femoral cutaneous nerve and the ilioinguinal and genitofemoral nerve in certain cases, and diaphragmatic breathing training. All patients completed physical therapy once a week for the entire protocol as evidenced by the physical therapy notes in their chart.

The data were analyzed using a Student's *t*-test. The statistical analysis using the *t*-test allowed us to compare the average values of the two data sets and determine if they came from the same population. In our analysis, the *t*-test took a sample from each of the two sets and established the problem statement by assuming a null hypothesis that the two means are equal. Based on the applicable formulas, certain values were calculated and compared against the standard values, and the assumed null hypothesis was accepted or rejected.

Outcome Measures

Response to treatment was measured before treatment and 3 months after treatment, using the 0 to 10 Visual Analogue Scale (VAS) to quantify their pelvic pain and the Functional Pelvic Pain Scale (FPPS) to assess function. For the VAS, the patients were asked to rate their average pain intensity over the past 24 hours. The FPPS rates pelvic function in eight categories: bladder, bowel, intercourse, walking, sleeping, working, running, and lifting. The patient rates each category from 0 to 4, with 0 being normal function, and 4 being severe debilitation. Thus, each patient can be given a total score from 0 to 32.

Results

Sixteen female patients underwent ultrasound-guided pelvic-floor trigger-point injections and peripheral nerve hydrodissection. Patients returned to work the same day of the procedure. No adverse events were noted. Follow-up data were measured up until 3 months post-treatment. The mean age of patients was 32.4 years (standard deviation [SD] 2.7) and the mean duration of pain was 6.7 years (SD 2.0). Table 2 demonstrates the range of pre- and posttreatment VAS scores for individual patients. Pretreatment, the mean VAS score was 6.0 (SD 2.7) and posttreatment the mean VAS score decreased to 2.9 (SD 2.6); $P < .05$, 95% confidence interval [CI] 1.16 to 4.97. Figure 2 demonstrates the average VAS and FPPS before and after treatment. The mean total FPPS score before treatment was 14.4 (SD 5.2) and posttreatment dropped to 9.1 (SD 5.8); $P < .05$, 95% CI 1.34 to 9.28. Analysis of the subcategories within the FPPS indicated that the improvement was statistically significant in the categories of intercourse, sleeping, and working. Figure 3 demonstrates the change in FPPS in the individual subcategories. In the category of intercourse, the mean change in score after treatment was 1.3 ($P < .05$, 95% CI 0.26-2.31). In the category of sleeping, the mean change in score after treatment was 1.2 ($P < .05$, 95% CI 0.32-1.99). In the category of working, the mean change in score after treatment was 0.9 ($P < .05$, 95% CI 0.18-1.53).

Table 2
Pretreatment and 3-month posttreatment pelvic pain intensity visual analogue scale (VAS) scores for individual participants

Patient #	Pretreatment VAS score	Posttreatment VAS score
1	6	2
2	6	3
3	9	9
4	8	5
5	4	0
6	2	2
7	10	8
8	8	2
9	1	0
10	5	4
11	5	1
12	7	2
13	3	3
14	7	3
15	10	3
16	5	0

Discussion

Our study evaluated the effectiveness of ultrasound-guided pelvic-floor trigger-point injections and peripheral nerve hydrodissection, in conjunction with physical therapy, in patients with a history of endometriosis. Both the mean VAS and FPPS scores decreased significantly by 3 points and 5 points, respectively, as shown in Figure 2. The treatment was safe and we observed no immediate complications.

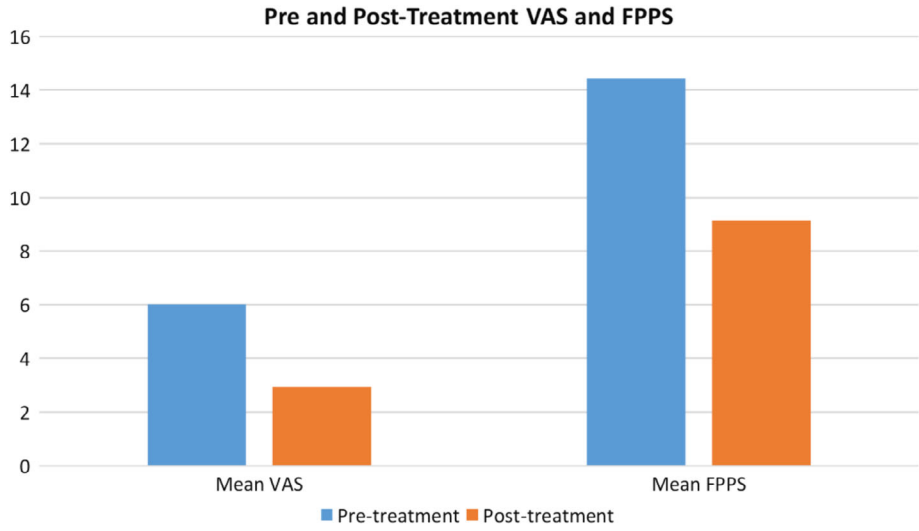

Figure 2. Pretreatment and posttreatment mean visual analogue scale (VAS) and functional pelvic pain scale (FPPS).

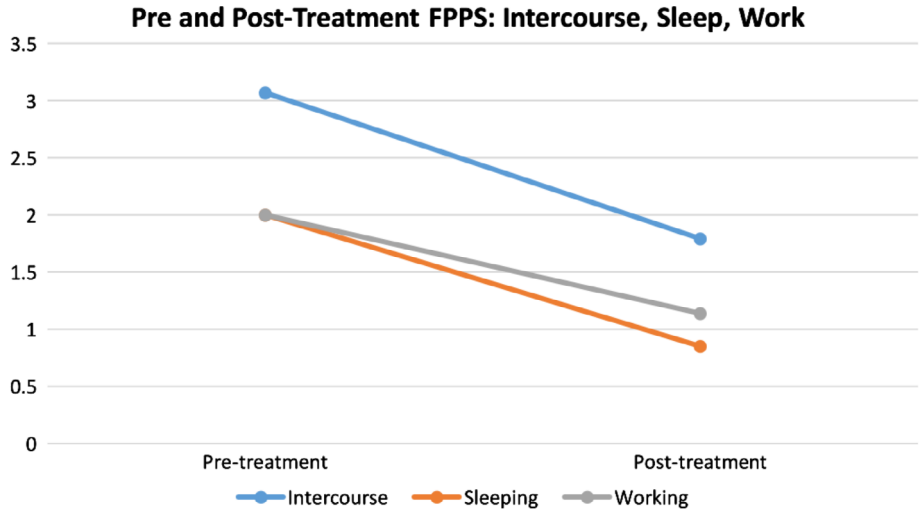

Figure 3. Pretreatment and posttreatment mean functional pelvic pain scales (FPPS) in the intercourse, sleep, and work subcategories.

The theory behind the treatment protocol is a three-prong approach to treat myofascial pain, neurogenic inflammation, and central sensitization, essentially breaking the pain cycle. The first part of the approach is to create space and increase blood around peripheral pelvic nerves via a peripheral nerve hydrodissection technique in combination with posttreatment nerve gliding with physical therapy. This increase in blood flow normalizes the local pH of the pelvic floor environment, which ultimately acts as a negative feedback for the stimulation of the inflammatory cascade. The second part is to desensitize hyperactive peripheral nociceptors and stop aberrant firing of these nerves. Lidocaine 1% is an Na channel blocker, and in chronic pain there is evidence that hyperactive sodium channels have a role in the aberrant firing of these nerves.[33] Therefore, repetitive use of an Na channel blocker will desensitize and ultimately reset aberrant peripheral nerves. In addition, lidocaine itself has some antiinflammatory properties.[34] The third aspect of the treatment protocol utilizes trigger-point injections and resets a short, contracted, weak muscle spindle. In addition, several studies have demonstrated decreasing the aberrant firing of peripheral nerves, which will then decrease the abnormal signaling to the spinal cord and brain, and ultimately decrease central sensitization.[35]

In women with a history of endometriosis, the location of the ectopic lesions does not necessarily correspond with the areas that women identify as most painful.[15] Given that the aim of traditional treatment, such as surgical resection and hormonal therapy, is to target these lesions, additional modalities are needed for pain control.[15] Myofascial dysfunction and associated trigger points contribute to CPP and have been associated with endometriosis.[15] A trigger point injection is thought to cause a mechanical interruption to the hypercontracted fibers via the needle itself and a blockade of pain signals via the substance injected.[15] Although limited, there are previous studies in the literature that suggest a

benefit of pelvic-floor trigger-point injections.[36] Bartley et al retrospectively studied 101 women who had received pelvic-floor trigger-point injections and noted improvement in 77% of patients.[36] Fouad et al reviewed VAS scores in 75 women before and 1 to 2 weeks after trigger-point injections, finding improving in 63% of patients.[37] Langford et al reported an improvement in 72% of women undergoing pelvic-floor trigger-point injections.[38] In our study, trigger-point injections contained lidocaine with dexamethasone and lidocaine with Traumeel and were performed via ultrasound guidance.

In addition to nociceptive pain, myofascial trigger points can contribute to centralized pain, or the sensitization of the CNS that is seen in endometriosis.[15,39] Centralized pain can be thought of as a maladaptive CNS response to continuous pain signals from the pelvis.[5] With these abnormalities in pain signal transmission, symptoms may be out of proportion to the stimulus and not correlate with the expected dermatomal patterns.[6] This central amplification in pain processing is thought to be responsible for accompanying somatic symptoms such as fatigue and sleep disturbance.[5] The statistically significant improvement seen in the FPPS categories of sleeping and working demonstrates effectiveness of our treatment regimen in addressing these centralized pain components. In addition, there can be a sensitization and subsequent hyperalgesia of neighboring pelvic structures that further contributes to this complex pain pattern.[5] Given that hydrodissection separates the nerve from adjacent structures, it may be considered effective in mitigating this cross-organ sensitization.[30]

Furthermore, as mentioned previously, pelvic nerves can be irritated by endometrial lesions or become entrapped by postoperative scar tissue, further contributing to central sensitization and subsequent pain.[6] Although the literature is sparse, there are case studies demonstrating ilioinguinal, iliohypogastric, and pudendal nerve entrapments after abdominal and cystocele surgeries, with pain symptoms abating after suture removal. In addition, given its anatomic location, the pudendal nerve may be compressed between the sacrospinous and sacrotuberous ligaments or along any of its branches by pelvic floor muscle spasm from chronic guarding.[6] Given the possibility of nerve invasion and/or entrapment in women with endometriosis, decompressive interventions may be effective. A paper by Robert et al found a 70% improvement in pudendal neuralgia after decompression.[40] Although not surgical decompression, hydrodissection is a much less invasive modality with a similar goal of creating space for the pudendal nerve. Finally, physical therapy, being a manual technique with minimal risk, may be beneficial with myofascial dysfunction and connective tissue release, dampening ectopic nerve activity.

We propose that if pain persists after resection of endometriosis and optimization of hormonal management of the disease, it is important to think of treating the myofascial pain, neurogenic inflammation, and central sensitization associated with CPP.

Our treatment protocol consisting of a combination of trigger-point injections, peripheral nerve hydrodissection, and pelvic-floor physical therapy was a multimodal approach aimed at the multiple facets that contribute to pelvic pain. To our knowledge, this is the first study that examined the effectiveness of these three modalities in conjunction with CPP in women with a history of endometriosis.

Some limitations of our study include a small sample size, short follow-up, and no control group. In addition, multiple treatments were used together, including use of combined 1% lidocaine with dexamethasone, then 1% lidocaine with Traumeel, peripheral nerve hydrodissection, and pelvic floor physical therapy, making it difficult to evaluate their individual merit. Patients were advised to continue their current medication doses during the study. This study opens the door to future studies investigating the long-term durability of this multifaceted treatment and/or the effectiveness of each individual treatment modality.

Conclusion

This study shows the effectiveness of detailed pelvic floor evaluations, pelvic floor musculature trigger-point injections, peripheral nerve hydrodissection, and physical therapy as a multimodal treatment option for patients with a history of endometriosis. Analysis suggests that the treatment was effective at relieving pain related to endometriosis; it also reflected promise in improving overall pelvic function, particularly in relation to intercourse, working, and sleeping. This study provides the foundation for future research with larger sample size and longer follow-up.

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Disclosure

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