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A novel, nonopiod-based treatment approach to men with urologic chronic pelvic pain syndrome using ultrasound-guided nerve hydrodissection and pelvic floor musculature trigger point injections

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Abstract

Introduction: Urological chronic pelvic pain syndrome (UCPPS) represents a group of pain symptoms relating to patients with pelvic pain for which treatment is largely unsatisfactory. The objective of this study is to analyze the effects of a novel treatment strategy in males suffering from UCPPS.

Methods: This retrospective, institutional review board–approved study analyzed eight male patients aged 24 to 61 with UCPPS. All the patients had a trial of antibiotic therapy, NSAIDs, and pelvic floor physical therapy before the study. The Visual Analog scale (VAS) and Functional Pelvic Pain scale (FPPS) were collected pretreatment. While continuing physical therapy, patients underwent weekly ultrasound-guided pelvic floor trigger point injections to the iliococcygeus, pubococcygeus, and puborectalis with lidocaine 1%. Concomitantly, patients received peripheral nerve hydrodissection performed on the pudendal nerve and the posterior femoral cutaneous nerve. The first two injections combined 1% lidocaine with dexamethasone, while the next four injections consisted of 1% lidocaine with traumeel (a homeopathic, plant-derived anti-inflammatory medication). At the 6-week follow-up, each patient retook the VAS and FPPS.

Results: The mean age of our patients was 31.8 years and the average duration of symptoms of the UCPPS was 21 months. Pretreatment, the mean VAS was 3.3 (STD 1.7) and the mean VAS posttreatment was 1.8 (STD 1.4); $P < .05$; 95% CI, 0.73 to 2.27. The mean FPPS pretreatment was 11.0

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(STD 8.0) and the mean FPPS posttreatment was 6.3 (STD 5.3); $P < .05$; 95% CI, 0.03 to 9.22.

Conclusion: Our results show promise for a novel, nonopioid-based treatment for UCPPS.

KEYWORDS

bladder, collagen, cystometry, cystostomy, HE staining, Masson staining, rat

1 | INTRODUCTION

Urological chronic pelvic pain syndrome (UCPPS) is newer nomenclature that has combined chronic prostatitis/chronic pelvic pain syndrome and interstitial cystitis, which are two of the most prevalent chronic urological pain disorders. According to the NIH, urologic chronic pelvic pain syndrome is broken down into four categories: acute bacterial prostatitis, chronic bacterial prostatitis, chronic pelvic pain syndrome, and asymptomatic inflammatory prostatitis.[1] UCPPS affects 2% to 16% of men worldwide.[2] In the United States, roughly 5% of all ambulatory care visits were related to genitourinary symptoms. Two million cases of which were diagnosed with prostatitis.[2] However, the diagnosis of prostatitis is often given in the setting of a normal urological work-up when a diagnosis of UCPPS is more appropriate.

The NIH classification for UCPPS has the following four categories.

- Category I—Acute bacterial prostatitis.
- Category II—Chronic bacterial prostatitis (CBP).
- Category III—Chronic pelvic pain syndrome (CPPS).
- Category IV—Asymptomatic inflammatory prostatitis.

Category II refers to patients with recurrent urinary tract infections suggesting a prostate nidus of infection.

Category III, CPPS, is now the most commonly diagnosed type of prostatitis. In this category, pain is the main symptom in prostatitis without uropathogenic bacteria. It is subdivided into category IIIA, inflammatory CPPS, which is identical to nonbacterial prostatitis and category IIIB, noninflammatory CPPS, which is identical to prostodynia.[3,4]

Category IV refers to an inflamed prostate without evidence of infection or symptoms.

Men with urological CPPS typically present with pain in the perineum, lower abdomen, testicles, and penis. The pain is often worse with ejaculation. The pathophysiology and etiology of UCPPS is unknown and is most likely a complex interplay of several factors. One hypothesis is that the signs and symptoms of UCPPS are due to an initiating stimulus such as infection, reflux of some toxic or immunogenic urinary substance, or perineal or pelvic repetitive microtrauma. This starts a cascade of events in an anatomically or genetically susceptible male, resulting in a local response of inflammation or neurogenic injury as a final common pathway. The result is the clinical manifestation of chronic perineal or pelvic pain and associated symptoms with local and central neuropathic mechanisms sometimes involving areas outside the prostate or pelvis.[5]

UCPPS treatment is empirical, with unsatisfactory patient outcomes.[6] Current treatment options in UCPPS include antibiotics for infection. Antibiotics target infection, inflammation, and voiding difficulties. In addition, anti-inflammatories and alpha blockers are often used in UCPPS treatment. Opioids are not standard of care for treatment for UCPPS.[7] Nonpharmacological treatments include acupuncture, physical therapy, and trigger point release. Physical therapy also plays an important role in UCPPS. Pelvic floor physical therapy consists of muscle control exercises, biofeedback, manual therapy, acupressure, nerve gliding, muscle energy, and mobilization techniques.[8] Pelvic floor physical therapy has been shown to significantly improve symptoms in women with pelvic floor myofascial pain. Furthermore, pelvic floor physical therapy for pelvic floor muscle hypertonia has been shown to alter local arterial blood flow to improve pelvic floor pain and UCPPS symptoms in men.[9] Trigger point injections in women with chronic pelvic pain have been shown to have positive results.[10] Moreover, trigger point injections to the pelvic floor musculature, consisting of iliococcygeus, pubococcygeus, and puborectalis muscles, can potentially treat myofascial dysfunction in the pelvic floor. (Figure 1)

Our treatment protocol aims at treating the myofascial pain and neurogenic inflammation concomitantly, ultimately decreasing the upregulation of the central nervous system. The protocol we propose uses a peripheral nerve hydrodissection technique, which is a type of procedure that removes adhesiolysis by introducing anesthetic or saline under pressure into planes of dissection.[11] The technique uses an anesthetic solution to separate the nerve from its adjacent fascia or muscle to decrease nerve hypersensitivity and create space and ultimately

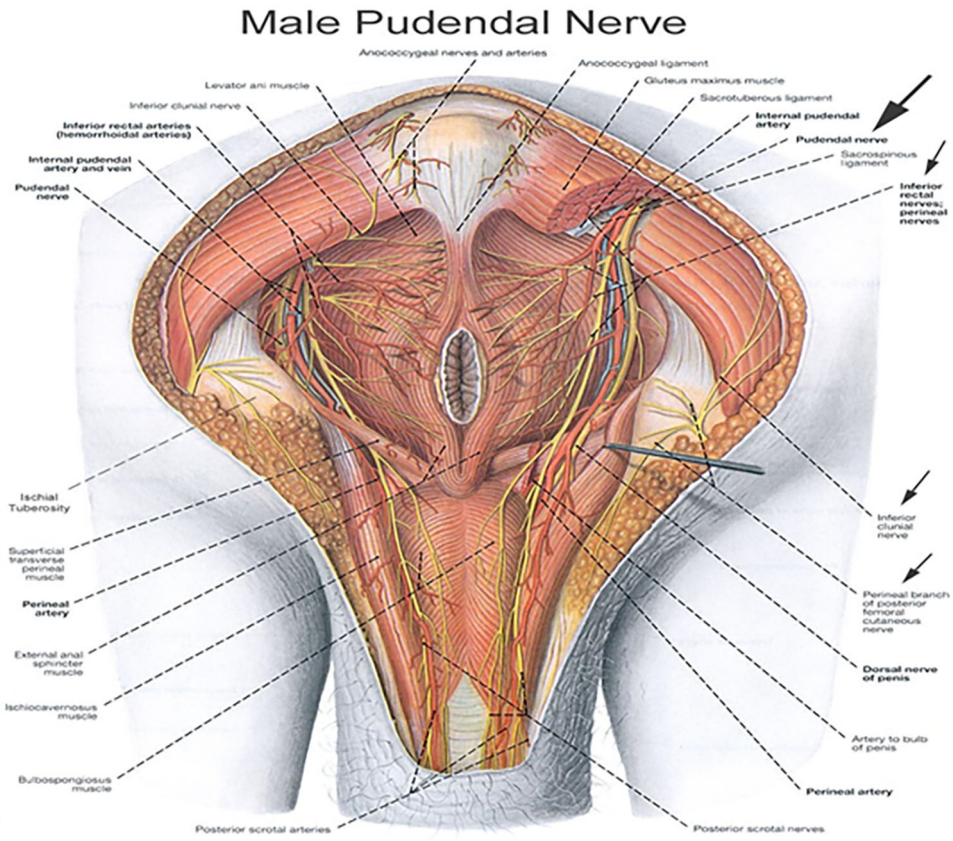

FIGURE 1 Male pelvic anatomy

improve blood flow around the nerve which will secondarily decrease neurogenic inflammation. Our protocol addresses neural sensitization as this is considered a central event in the pathogenesis of CPPS.[12]

TABLE 1 Patient population and demographic data (n = 8)

Average age	30.25
Average duration of pain	3.88 y
Relevant medical comorbidities	
Hip labral tears	N = 3
Lumbar radiculopathy	N = 2
Testicular cancer	N = 1
Anxiety/depression	N = 1
Fibromyalgia	N = 1
Failed medications	
Opioid medications	N = 2
Duloxetine	N = 4
Pyridium	N = 3
Gabapentin	N = 1
Silodosin (Rapaflo)	N = 1
Pregabalin (Lyrica)	N = 1
Tricyclic antidepressants	N = 2
Previous interventions	
Epidural steroid injections	N = 3
Nerve blocks	N = 1
Antibiotic prostate injections	N = 1
Competitive athletes	N = 5

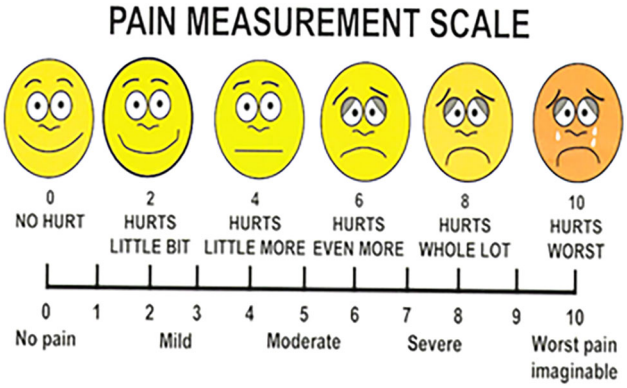

FIGURE 2 Visual Analog scale

2 | METHODS

This retrospective, institutional review board–approved study from May 2017 to May 2018 analyzed eight male patients aged 24 to 61 with UCPPS (Table 1). All patients had a trial of NSAIDs in combination with antibiotic therapy, and had pelvic floor physical therapy pre- and posttreatment. Patients' scores on the Visual Analog scale (VAS) and Functional Pelvic Pain scale (FPPS) were collected pretreatment (scales are noted in Figures 2 and 3). While continuing physical therapy, patients

FUNCTIONAL PELVIC PAIN SCALE

Name:_____ Date:_____

INSTRUCTIONS: Please fill out this form by placing an **X** in the box that best describes your pain when it is the **WORST**, even if it occurs at different times of your cycle.

If any of these functions do not apply to you, please write **N/A** (not applicable) in the box beside that function.

Function	0 No Pain, Normal Function	1 Some Pain with Function	2 Moderate Pain with Function	3 Severe Pain with Function	4 Incapable of Function because of Pain
Bladder					
Bowel					
Intercourse					
Walking					
Running					
Lifting					
Working					
Sleeping					

FIGURE 3 Functional Pelvic Pain scale

underwent weekly external ultrasound-guided pelvic floor trigger point injections using a 27 gauge spinal needle to the iliococcygeus, pubococcygeus, and puborectalis. The first two injections combined 1% lidocaine with dexamethasone, while the next four weekly injections consisted of 1% lidocaine with traumeel, a plant-derived anti-inflammatory medication and its components are described in Figure 4.[13]

Concomitantly, patients received ultrasound-guided peripheral nerve hydrodissection performed on the pudendal and the posterior femoral cutaneous nerve. Hydrodissection involves injection of saline or fluid to create space around the nerves, separating them from surrounding fascia and adjacent structures. These treatments lasted for 6 weeks. After completion of treatment, a 6-week follow-up was scheduled and each patient retook the VAS and FPPS.

2.1 | Inclusion criteria

Adult male patients aged 18 years or more presenting with the following symptoms.

1. Pain in one or more locations—groin, scrotum, penis, perineum, suprapubic, low back, and/or anus for majority of time in the last 3 months or more.
2. Along with the above, the presence of one or more of the following:
   - Dysuria.
   - Ejaculation pain.
   - Lower urinary tract symptoms involving storage or voiding of urine.
   - Erectile dysfunction.
3. Completion of a course of antibiotics (2-12 weeks)/ NSAID combination.
4. Completion of 8 to 12 weeks of pelvic floor physical therapy.
5. All patients underwent a complete urological workup described below. These tests were performed by a urologist before patient consultation with the physiatrist. The urologic workup was normal for all patients.
   - Urinalysis.
   - Midstream culture.
   - 2-glass prostate test.
   - Prostate ultrasound.

Components of Traumeel (eg, ointment, tablets, and ampoules)

Source of extract	Characteristics[a]
Achillea millefolium (milfoil)	Hemorrhages, especially precapillary arteriovenous (anastomosis), oozing hemorrhages
Aconitum napellus (monkshood)	Fever with hot, dry skin, neuralgia, inflammatory rheumatism; improvement of the vasotonia; analgesic, hemostatic
Arnica montana (mountain arnica)	To stimulate the healing of wounds, fractures, dislocations, contusions, hemotomas, myocardial weakness, neuralgia, myalgia, analgesic, hemostatic
Atropa belladonna (deadly nightshade)	Localized reaction phases, cerebral sensitivity with cramp and delirium
Bellis perennis (daisy)	Dislocations, contusions, sensation of soreness in the abdominal wall/cavity, exudative processes, resorption of edema
Calendula officinalis (calendula)	Slowly healing wounds, promotes granulation, analgesic
Matricaria recutita (chamomile)	Anti-inflammatory; stimulates granulation, promotes healing in difficult healing wounds and ulcers; fistulae, hemorrhoids, mastitis, intertrigo, aphthous stomatitis, conditions of restlessness and excitation, disorders of dentition, otitis media, glandular swellings
Echinacea angustifolia (narrow-leaved cone flower)	Increase in the mesenchymal defences; inflammation of all kinds and locations; septic processes; hyaluronidase inhibiting, anti-inflammatory action
Echinacea purpurea (purple cone flower)	Increase in the mesenchymal defences; inflammation of all kinds and locations; septic processes; hyaluronidase inhibiting, anti-inflammatory action
Hamamelis virginiana (witch hazel)	Venous stasis, varicose veins, (thrombo-) phlebitis, crural ulcers, hemorrhoids, venous hemorrhages, anti-inflammatory, analgesic
Calcium sulphide (otherwise: Hepar sulfuris)	Tendency to suppuration, especially on the skin and lymph glands (furuncles, pyodermia, panaris, phlemons), tonsillar abscesses, chalazions, hordeolums, hemicrania, urinary disorders, hypersensitivity to cold and draughts
Hypericum perforatum (St John's wort)	Neural and cerebral injuries, eg, commotio cerebri neural pains upon or after injuries hemostatic
Mercurico-amidonitrate (otherwise: *Mercurius solubilis Hahnemanni*)	Suppurations, abscesses, gingivitis, stomatitis, nasopharngeal catarrh, catarrh of the sinuses, cholangitis, shrinking action on edematous conditions
Symphytum officinale (comfrey)	To accelerate callus formation in fractures periostitis, causalgia, disorders arising from amputation stumps contusions
Excipients	–

FIGURE 4 Properties and ingredients of traumeel

2.2 | Exclusion criteria

1. Active infection.
2. History of metastatic bone cancer.
3. History of pelvic fracture.
4. Interstitial cystitis.

2.3 | Statistical analysis

In view of the small sample size and retrospective nature of the study, the data were analyzed using the Student *t* test with *a P* value of less than .05 correlating with a statistical difference.

3 | RESULTS

Our study included eight male patients aged 24 to 61 with diagnosed UCPPS. The mean age was 31.8 years and each subject was treated with pelvic physical therapy, trigger point injections, and nerve hydrodissection. Zero patients were lost to follow up. Each patient tolerated the 6-week sessions of hydrodissection and trigger point injections without significant adverse events. We measured pain results based on the VAS and overall function was based on the FPPS. The FPPS is a 5-point scale (0-4) that measures function in relation to these factors: bladder, bowel, intercourse, walking, running, lifting, working, and sleeping. Before initiation of treatment, subjects had a mean VAS of 3.3 with a standard deviation of 1.7. At the 6-week follow-up postprotocol, the mean VAS was 1.8 with a standard deviation of 1.4 ($P < .05$; 95% CI, 0.73-2.27). The mean FPPS before the treatment was 11.0 with a standard deviation of 8. At the 6-week follow-up, the mean FPPS improved to 6.3 with a standard deviation of 5.3 ($P < .05$; 95% CI, 0.03-9.22) in Figure 5. There was a statistically significant improvement in pain at the 6-week follow-up examination.

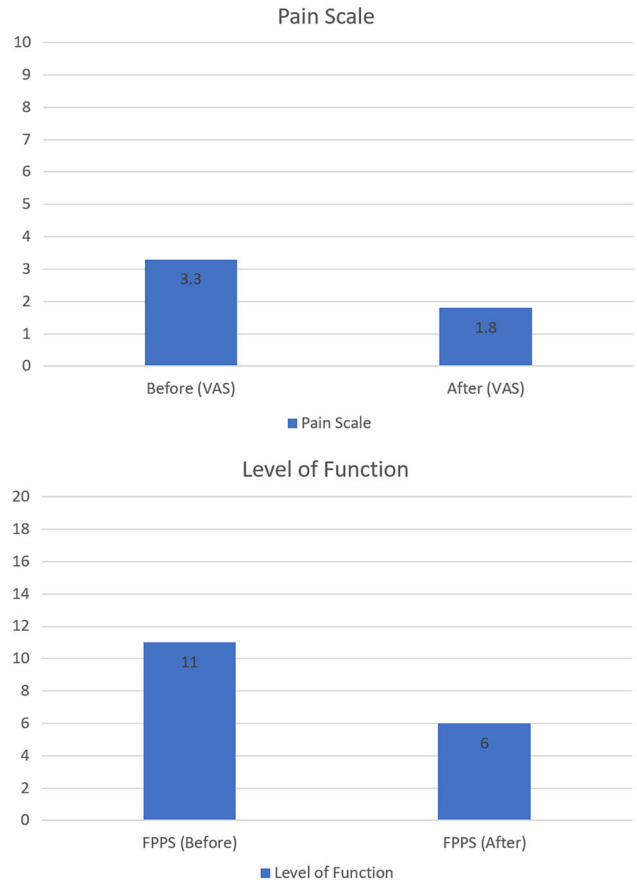

FIGURE 5 A, VAS pre- and posttreatment. B, FPPS pre- and posttreatment. FPPS, Functional Pelvic Pain scale; VAS, Visual Analog scale

4 | DISCUSSION

UCPPS is considered to have a significant component of central and peripheral neuropathic hypersensitization.[14] In addition, up to 85% of men with chronic pelvic pain may have pelvic floor tenderness[15] and these areas of tenderness reproduce the patient's pain with palpation in many cases.[16] Currently, there is no standard treatment algorithm for UCPPS.

It is generally agreed upon that clinicians take a broad approach to defining UCPPS. UCPPS is not a homogenous group of patients with prostate, bladder, and pelvic pain. UPOINT, which is an acronym for urinary, psychosocial, organ specific, infection, neurologic/systemic, and tenderness, represents a six-point characterization system that was developed to facilitate multifacet treatment approaches to UCPPS.[17] Pelvic floor therapy is the initial mainstay of therapy but beyond this, there is little evidence for the best next step in treatment. The treatment protocol described includes a three-pronged approach to treat the myofascial pain, neurogenic inflammation, and central sensitization addressing the potential underlying pathophysiology of UCPPS.

In this retrospective trial, eight male patients with UCPPS were treated with a combination of pelvic floor physical therapy, pelvic floor trigger point injections, and hydrodissection of the pudendal nerve and posterior femoral cutaneous nerve. Both the VAS and FPPS had statistically significant improvement with the treatment protocol. The results show patients experienced improved overall pain and improvement in daily functions including bladder/bowel function, intercourse, walking, running, lifting, working, and sleeping.[18]

Hydrodissection is a therapy for adhesiolysis and nerve desensitization by introducing saline or anesthetic

under pressure into planes of dissection, ultimately increasing space for nerves to glide.[19] There is very little literature on the effectiveness of hydrodissection, especially targeting nerves causing pelvic pain. However, Clendenen et al (2015) performed hydrodissection followed by corticosteroid injection of the infrapatellar branch of the saphenous nerve in patients with chronic medial knee pain following total knee replacement.[20] The patients' VAS improved from a baseline of 8-10 to 3-4 at follow-up between 6 to 12 months.[20] Wu et al[21] performed a prospective, randomized, double-blinded controlled study comparing hydrodissection of the carpal tunnel with one 5-mL dose of normal saline to a control group. The intervention group had significantly greater improvement at the second and third month posttreatment month follow-up according to the Boston Carpal Tunnel Syndrome Questionnaire Score and 5-point Global Response Assessment.[21] Conceptually, desensitizing aberrant firing of peripheral nerves will not only help treat peripheral sensitization but also inhibit the feedback loop that drives central sensitization, as shown in fibromyalgia patients.[22] Trigger point injections to treat myofascial pain are commonly used in men with UCPPS. The mechanism of action of trigger point injections is not completely understood but it may include the interruption of the positive feedback loop that perpetuates pain. Its etiology is theorized to stem from metabolic imbalance at the peripheral myofascial tissue and this effect on the centralized pain phenomenon.[23] Based on these theories, trigger point injections could potentially address both peripheral and central sensitization of UCPPS. In a retrospective evaluation of patients who received at least 1 trigger point injection accompanied with a pudendal block or ilioinguinal block, Chronic Prostatitis Symptom Index scores dropped from an initial score of 28.8 to 21.8. This indicates improvement in pain, urinary symptoms, and quality of life.[10] Another study targeting levator ani trigger point injections in 18 women with chronic pelvic pain yielded a mean preinjection VAS of 88% with a 3-month postinjection VAS of 36%. Six of the 18 patients reported being completely pain free.[24] A randomized comparative study of pelvic floor physical therapy versus levator ani directed trigger point injections (LTPI) investigated their efficacy in treating levator-related pelvic pain and sexual function. Both groups reported reduction of vaginal pain with no significant difference between the two groups in the percentage of patients reporting greater than 50% improvement (59% of PT and 58% of LTPI). However, the change in the Numeric Rating scale (NRS) per treatment session favored LTPI. We propose the combination of pelvic floor physical therapy and LTPI may lead to more significant and faster improvement in NRS compared with each treatment alone.

Our study is the first of its kind looking at possible synergistic effects of pelvic floor physical therapy, trigger point injections, and nerve hydrodissection in patients with UCPPS. It may be advantageous to consider initiating treatment of UCPPS with this three-prong approach in patients who plateau or fail to progress after 8 to 12 weeks of pelvic floor physical therapy alone. Some limitations of our study include a small sample size, retrospective in nature, 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, trigger point injections, and pelvic floor physical therapy, making it difficult to evaluate their individual merit. 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.

5 | CONCLUSION

Our results show promise for a novel, nonopioid-based treatment for UCPPS by using ultrasound-guided pelvic floor trigger point injections combined with peripheral nerve hydrodissection with lidocaine, traumeel, and dexamethasone along with a pelvic floor physical therapy program.

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