


The Role of Acupuncture and Its Related Mechanism in Treating Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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Abstract: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is one of the most common diseases in urology, and its prevalence has been increasing, causing serious urogenital problems in men. Several targeted oral drug therapies exist to treat the pelvic pain experienced in this disease. However, these therapies may have potential adverse effects, and due to the unique location of the prostate, delivery of medications to the target lesion is difficult. Consequently, many patients seek alternative therapies. Acupuncture is a well-established treatment method in traditional Chinese medicine that can improve CP/CPPS symptoms and reduce pain. However, previous systematic reviews overlooked the significance of the characteristics and mechanisms of acupuncture therapy. This study aimed to summarize the characteristics and benefits of acupuncture therapy for CP/CPPS based on relevant literature and predict and analyze its related mechanisms.

Keywords: acupuncture, chronic prostatitis, chronic pelvic pain syndrome, mechanism, traditional Chinese medicine, pain

Introduction

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) refers to urologic pain or discomfort in the pelvic region, as defined by the National Institutes of Health (NIH). It primarily presents no urinary tract infection for at least 3 months in a 6-month period.¹ CP/CPPS affects approximately 2–15% of adult men of all ages, particularly those in their middle age, and the chronic symptoms usually last up to 6 months or longer.^{2–4} Chronic pain, the most common symptom of CP/CPPS, is difficult to treat and often affects patients' daily lives, leading to negative emotions and sexual dysfunction.^{5,6} Considering the complexity of CP/CPPS, mental issues, stress and previous prostatic infections may be its etiology and risk factors.^{7,8}

The primary goal of CP/CPPS treatment is to alleviate pain and reduce urination symptoms to improve patients' quality of life.⁹ However, no unified treatment strategy has been developed.¹⁰ Several treatments are available for CP/CPPS, but due to the unique anatomical functional structure of the prostate tissue, many drugs are unable to cross the blood–prostate barrier. The current treatment strategy mainly aims to alleviate clinical symptoms, but its efficacy is not very satisfactory.¹¹ Antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs), neurotransmitter antagonists, allopurinol, and botanicals can alleviate clinical symptoms and lower the NIH-chronic prostatitis symptom index (NIH-CPSI) score and its associated pain subscore.¹² However, these drugs must be taken for an extended period of time and have several adverse effects and a high recurrence rate.^{13,14} Considering that no established treatment is valid for all patients, the role of acupuncture could enrich the multidisciplinary approach of this condition.

Acupuncture is also a non-oral drug therapy, which is a critical component of traditional Chinese medicine (TCM). And it has been extensively used to treat various pain-related and urological diseases,^{15,16} with the majority of studies focusing on CP/CPPS.¹⁷ Unlike other systematic reviews,^{18–20} we reviewed previous clinical evidence to analyze factors,

such as acupoint selection, needle retention time, and duration of acupuncture therapy, and discussed the characteristics and mechanisms of acupuncture therapy to provide a reference for future treatment of CP/CPPS using acupuncture.

Materials and Methods

Search Strategy

The PubMed, Embase, and Cochrane Library databases were searched for relevant studies (up to October 2022). We also reviewed the reference lists of the studies identified via our search strategy and selected those that seemed relevant based on our keywords. The search was conducted in English. The following search terms were used: acupuncture, acupuncture treatment, electroacupuncture, acupuncture therapy, fire needling, scalp acupuncture, ear acupuncture, prostatitis, chronic pelvic pain syndrome, nonbacterial prostatitis, chronic prostatitis, clinical trial, clinical article, clinical study, controlled study, and randomized controlled trial (Table 1).

Inclusion Criteria

1. Study types: Clinical trials involving acupuncture for CP/CPPS were included, and the qualified papers were limited to the English language.
2. Participants: Patients with CP/CPPS (as defined by the NIH) were included, regardless of their ethnicity, country, and course.
3. Intervention types: Common acupuncture (including electroacupuncture, fire needling, scalp acupuncture, and ear acupuncture) alone without other pharmacotherapies and external treatments in the treatment group, regardless of acupoint position, treatment frequency, and course. The establishment of a control group was not required.
4. Comparison types: The control group received conventional treatment, medication, placebo acupuncture, sham acupuncture, or no treatment. Or there were no control groups.
5. Outcome types: Changes in the total NIH-CPSI score and NIH-CPSI pain domain subscore were recorded as outcomes.

Table 1 PubMed Search Strategy

No.	Search Item
#1	Acupuncture [Title/Abstract]
#2	Acupuncture treatment [Title/Abstract]
#3	Electroacupuncture [Title/Abstract]
#4	Acupuncture therapy [Title/Abstract]
#5	Fire needling [Title/Abstract]
#6	Scalp acupuncture [Title/Abstract]
#7	Ear acupuncture [Title/Abstract]
#8	Or/#1-#7
#9	Prostatitis [Title/Abstract]
#10	Chronic pelvic pain syndrome [Title/Abstract]
#11	Nonbacterial prostatitis [Title/Abstract]
#12	Chronic prostatitis [Title/Abstract]
#13	Or/#9-#12
#14	Clinical trial [Publication Type]
#15	Clinical article [Publication Type]
#16	Clinical study [Publication Type]
#17	Controlled study [Publication Type]
#18	Randomized controlled trial [Publication Type]
#19	Or/#14-#18
#20	#8 and #13 and #19

Data Collection and Analysis

Selection of Studies

According to the search strategy, two authors searched for relevant articles and summarized the results. Duplicate studies were eliminated. Some studies were excluded after analyzing the title and abstract. Furthermore, studies that did not meet the inclusion criteria were eliminated after analyzing the full text. Dissenting opinions were submitted to another author for adjudication throughout the whole process (Figure 1).

Data Extraction

Two authors independently extracted data in a standard format. These data included the author, publication date, number of participants treated with acupuncture or EA, acupuncture points, acupuncture therapy types, session duration, and reported outcomes (Table 2). The two authors checked the extracted data for accuracy and completeness. Another author participated in discussions and helped resolve any disagreements.

Results

After duplicates were removed, only 692 of the 1298 searched studies were included in the assessment as shown in the selection flowchart (Figure 1). Following a review of the topics and abstracts, 631 studies were excluded because they

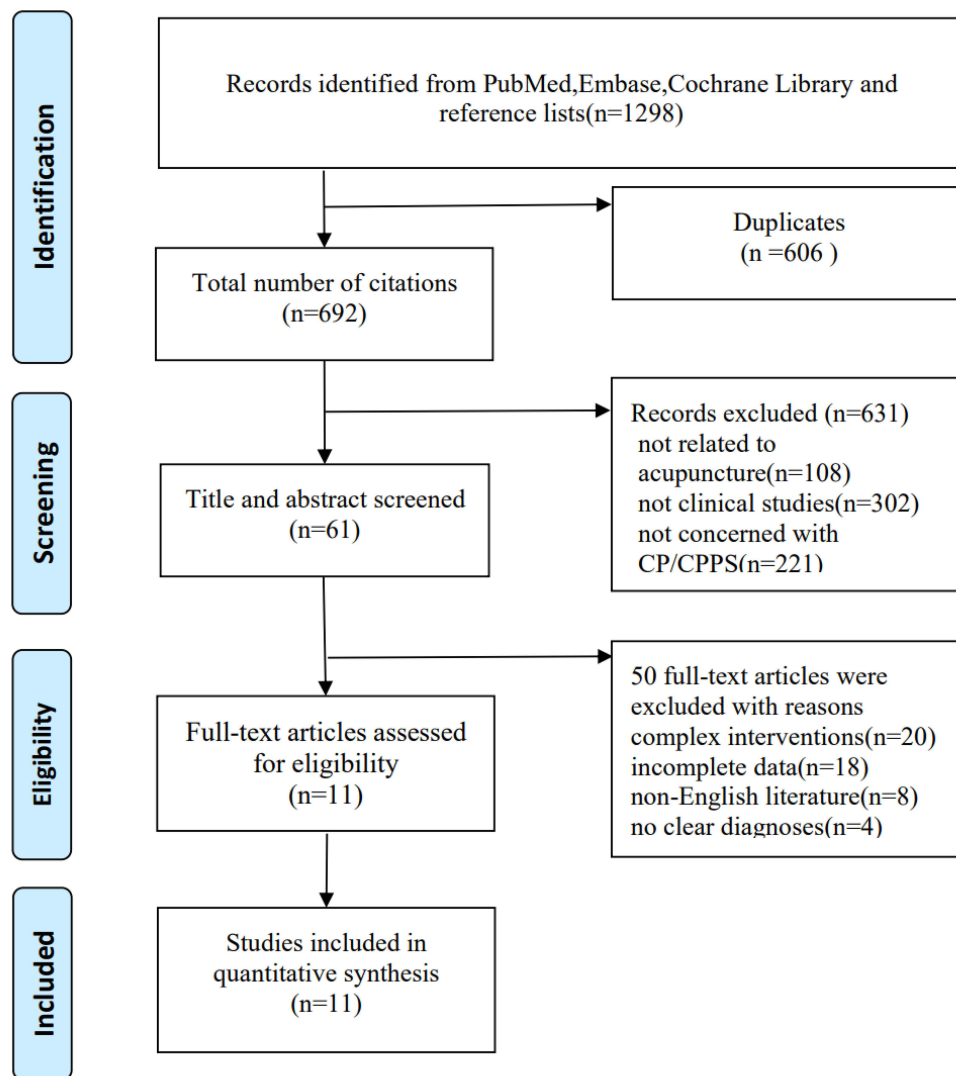


Figure 1 Flow chart of the study search.

Table 2 Summary of the Included Studies

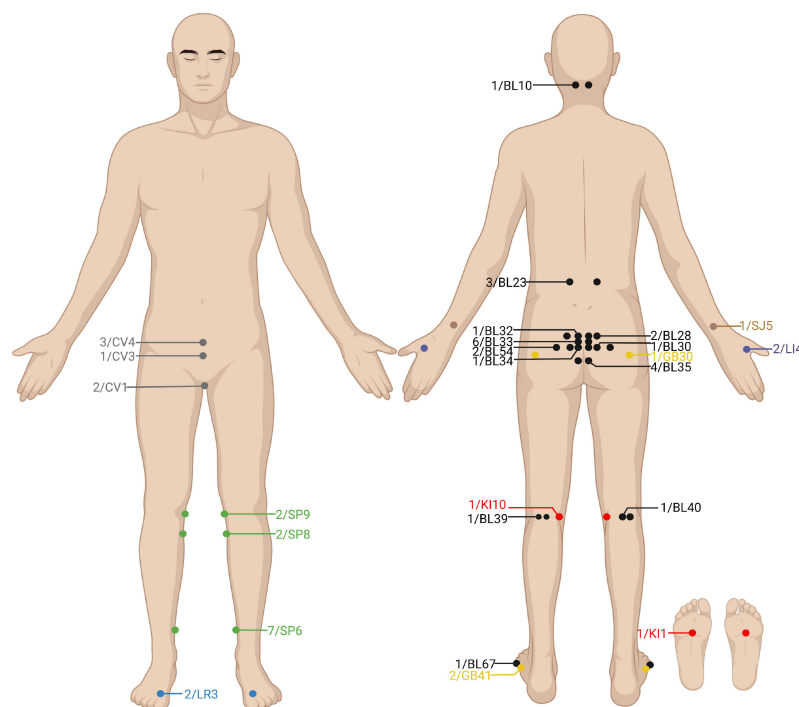
References	Sample	Acupuncture Points	Intervention	Pain	NIH-CPSI
Sun et al (2021) ²¹	220	BL33 (Zhongliao), BL35 (Huiyang), BL23 (Shenshu), SP6 (Sanyinjiao)	AC, 30 min 20 sessions over 8 weeks	16.4 ± 2.6 Adjusted mean change: -2.1 (-2.4 to -1.9)	31.0 ± 4.8 Adjusted mean change: -7.4 (-8.0 to -6.8)
Qin et al (2018) ²²	34	BL33 (Zhongliao), BL23 (Shenshu), BL35 (Huiyang), SP6 (Sanyinjiao)	AC, 20–25 min 3/week for 8 weeks	12.4 ± 2.8 to 6.9 ± 0.9	28.0 ± 4.8 to 17.0 ± 1.7
Zhou et al (2017) ²³	77	BL30 (Baihuanshu), BL35 (Huiyang)	EA, 30 min 6 sessions for 2 weeks	TA: 11.1 ± 2.8 to 6.6 ± 4.0 LA: 11.1 ± 3.1 to 3.3 ± 3.8	TA: 26.7 ± 4.9 to 17.3 ± 9.1 LA: 26.6 ± 5.8 to 9.4 ± 8.6
Sahin et al (2015) ²⁴	50	BL33 (Zhongliao), BL34 (Xialiao), BL54 (Zhibian), CV1 (Huiyin), CV4 (Guanyuan), SP6 (Sanyinjiao), SP9 (Yinlingquan)	AC, 20 min 1/week for 6 weeks	13.2 ± 2.3 to 6.14 ± 1.49	27.0 ± 3.5 to 10.84 ± 1.92
Kucuk et al (2015) ²⁵	26	BL28 (Pangguangshu), GB41 (Zulinqi), LR3 (Taichong), LI4 (Hegu), SP6 (Sanyinjiao), SP8 (Diji)	EA, 2/week for 7 weeks	11.07 ± 3.58 to 6.65 ± 3.73	20.36 ± 7.35 to 12.54 ± 4.95
Tugcu et al (2010) ²⁶	97	BL33 (Zhongliao)	AC, 20 min 1/week for 6 weeks	11.6 ± 2.2 to 5.9 ± 2.4	26.6 ± 2.9 to 10.6 ± 5.4
Lee et al (2009) ²⁷	12	BL32 (Ciliao), BL33 (Zhongliao), GB30 (Huantiao)	EA, 20 min 2/week for 6 weeks	12.2 ± 2.5 Variable: -5.2 ± 1.9	26.9 ± 5.2 Variable: -9.5 ± 3.7
Lee et al (2008) ²⁸	44	CV1 (Huiyin), CV4 (GuanYuan), SP6 (Saninjiao), SP9 (Yinlingquan)	AC, 30 min 2/week for 10 weeks	11.4 ± 3.4 to 7.0 ± 4.5	24.8 ± 6.2 to 14.5 ± 8.7
Capodice et al (2007) ²⁹	10	SJ5 (Waiguan), GB41 (Zulinqi), LR3 (Taichong), LI4 (Hegu), SP8 (Diji), SP6 (Sanyinjiao)	AC, 20–25 min 2/week for 6 weeks	9.9 ± 3.1 to 2.1 ± 2.0	25.1 ± 6.6 to 6.6 ± 4.3
Honjo et al (2004) ³⁰	10	BL33 (Zhongliao)	AC, 10 min 1/week for 5 weeks	Not reported	11.6 ± 4.5 to 8.8 ± 6.3
Chen et al (2003) ³¹	12	BL10 (Tianzhu), BL23 (Shenshu), BL28 (Pangguangshu), BL40 (Weizhong), KI10 (Yingu), KI1 (Yongquan), BL67 (Zhiyin), CV4 (Guanyuan), CV3 (Zhongji), SP6 (Sanyinjiao), BL54 (Zhibian), BL35 (Huiyang), BL39 (Weiyang)	AC + EA, 20 min 2/week for 6 weeks	14.1 ± 2.2 to 4.2 ± 2.9	28.2 ± 4.8 to 8.5 ± 5.1

Abbreviations: AC, acupuncture; EA, electroacupuncture; LA, long-needle acupuncture; TA, traditional acupuncture.

were not clinical trials or were unrelated to acupuncture or CP/CPPS. Furthermore, 50 studies were excluded after reading the full text due to complex interventions, incomplete data, non-English language, and unclear diagnosis. Finally, we included 11 English clinical studies involving 570 patients who received acupuncture or EA. Of the 11 studies included, 7 were randomized controlled trials (RCTs)^{21–25,27,28} and four were before-and-after studies in the same patient.^{26,29–31}

Various acupoint selection methods have been applied in the treatment of CP/CPPS, involving 25 different acupoints and 8 meridians, which include bladder meridian of foot-taiyang, ren meridian, kidney meridian of foot-shaoyin, gallbladder meridian of foot-shaoyang, spleen meridian of foot-taiyin, liver meridian of foot-jueyin, large intestinal meridian of hand-yangming, and triple energizer meridian of hand-shaoyang. Some similarities were observed among acupoint selection studies. Statistical analysis was used to examine the frequency of acupuncture points used in each study (Figure 2). The lumbosacral and lower extremities are the primary targets of acupuncture points. The acupoint meridians were primarily the bladder meridian of foot-taiyang (12/25), ren meridian (3/25), and spleen meridian of foot-taiyin (3/25). SP6 (Sanyinjiao) was the most frequently used acupoint (seven times), followed by BL33 (Zhongliao; six times), BL35 (Huiyang; four times), and BL23 (Shenshu; three times).

Acupuncture was used in seven studies,^{21,22,24,26,28–30} EA in three studies,^{23,25,27} and EA combined with acupuncture in one study.³¹ Except in Kucuk et al's study,²⁵ which did not specify the duration of each treatment, the duration of each acupuncture session was 10–30 min for 2–10 weeks. Each acupuncture session lasted 20 min in four studies,^{24,26,27,31} 30 min in two studies,^{23,28} and 20–25 min in another two studies.^{22,29} Honjo et al³⁰ treated CP/CPPS by giving acupuncture for 10 min per session. The sessions were repeated for 6 weeks in most studies^{24,26,27,29,31} and for more than 7 weeks in four studies.^{21,22,25,28} The frequency of the session was two or three times a week in eight studies^{21–23,25,27–29,31} and once a week in the remaining studies.^{24,26,30}



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Figure 2 The location and distribution of the acupoints. Created with BioRender.com.

Notes: The black, gray, red, yellow, green, blue, purple, and brown circles or lines represent the frequency/acupoint of bladder meridian of foot-taiyang, ren meridian, kidney meridian of foot-shaoyin, gallbladder meridian of foot-shaoyang, spleen meridian of foot-taiyin, liver meridian of foot-jueyin, large intestinal meridian of hand-yangming, and triple energizer meridian of hand-shaoyang, respectively.

All studies showed varying degrees of improvement in the NIH-CPSI score and its primarily associated pain subscore. The urinary subscore and quality-of-life subscore are also included in the NIH-CPSI scale. After acupuncture treatment, differences in the changes in NIH-CPSI scores and pain scores were noted across studies (Table 2). Notably, in the same study, the improvement in patients' NIH-CPSI scores and pain subscores varied at different time points and was represented in four studies. Sun et al²¹ reported that the adjusted mean change in NIH-CPSI scores was -4.8 (-5.4 to -4.3) at week 4 and that in the pain subscore was -1.6 (-1.8 to -1.3). Qin et al²² reported that the adjusted mean pain subscore was 8.9 (8.2 – 9.7) at week 4 and the NIH-CPSI total scores at week 4 were also higher than those at week 8. Lee et al²⁷ also assessed the efficacy of acupuncture for CP/CPPS at week 3, and the results showed that the adjusted mean change in NIH-CPSI scores was -7.0 ± 5.1 and that in the pain subscore was -3.7 ± 2.6 . Furthermore, according to the findings of Lee et al,²⁸ the mean NIH-CPSI score at week 5 was higher than that at week 10.

We also analyzed the situation in the period after the completion of the treatments. From Sun et al²¹ and Qin et al,²² the efficacy of acupuncture in reducing NIH-CPSI and pain subscore may persist until week 32. A 22-week follow-up from Zhou et al²³ also indicated both traditional acupuncture and long-needle acupuncture can significantly reduce NIH-CPSI and pain subscore ($P < 0.05$). At week 24 of following-up, success in acupuncture group was 74% in the study of Sahin et al.²⁴ Also, the effect of decreasing NIH-CPSI and pain subscore were also lasting at week 24 in another study.²⁶ These follow-up results all indicated a sustained effect of acupuncture.

Discussion

Characteristics of TCM and Its Use in Treatment

Shoskes et al³² proposed and formulated UPOINT, which is a significant research project following the NIH-CPSI. It classifies prostatitis into six clinical phenotypes: urinary symptoms, psychosocial, organ-specific, infection, neurological/systemic, and skeletal muscle tenderness. Personalized treatment based on UPOINT consists of several steps. In addition to health education, health consultation, reasonable exercise, anxiety reduction, and diet modification, conventional drugs, such as antibiotics and α -blockers, are used to treat CP/CPPS.³³ Similar to UPOINT, TCM emphasizes on the holistic concept and syndrome differentiation. Acupuncture, as an important component of TCM, is widely practiced and is recognized and accepted in many countries. The purpose of acupuncture is to alleviate symptoms through a holistic approach. Numerous studies have already shown that acupuncture can effectively improve UPOINT symptoms with few adverse effects. Furthermore, 11 studies in this review reported no serious adverse effects.

Acupoint Location

Meridian and acupoint selection in TCM includes proximal and distal acupoint selection.³⁴ Proximal acupoint selection is a common acupoint selection method, and proximal acupoints include BL30 (Baihuanshu), BL32 (Ciliao), BL33 (Zhongliao), BL34 (Xialiao), BL35 (Huiyang), and BL54 (Zhibian). These acupoints are concentrated in the lumbosacral region and are the most commonly used acupoints in this review (Figure 2). Acupuncture at BL32 (Ciliao) and BL33 (Zhongliao), which are located in the second and third posterior sacral foramina, respectively, and BL34 (Xialiao) and BL54 (Zhibian), which are located in the third and fourth posterior sacral foramen, respectively, can stimulate the sacral nerve segments and relieve pain via direct inhibition at the spinal cord level.²⁴ In particular, transsphenoidal sacral nerve stimulation has a beneficial effect on chronic refractory pelvic pain.²⁷ BL30 (Baihuanshu) and BL35 (Huiyang) are located near the pudendal nerve, which is the main sensory and motor nerve of the perineum, providing genital sensation as well as controlling the urethral sphincter and anal sphincter. In patients with CP/CPPS, acupuncture at these two acupoints stimulates the pudendal nerve, inhibits local sensory transmission to the central nervous system, and reduces pain symptoms.²³ In distal acupoint selection, acupoints far from the lesion site are selected. This selection method reflects the meridian theory of TCM. In this review, BL10 (Tianzhu), BL39 (Weiyang), BL40 (Weizhong), and BL67 (Zhiyin) were all on the bladder meridian of foot-taiyang, whereas SP8 (Diji), SP9 (Yinlingquan), and SP6 (Sanyinjiao), which are distributed below the knee joint, were all on the spleen meridian of foot-taiyin. Based on the meridian theory of TCM, the circulation of the bladder meridian of foot-taiyang and the spleen meridian of foot-taiyin passes through the lower abdomen or lumbar spine.

Retention Time

Each treatment in our study lasted for 10–30 min. The acupuncture effect is divided into three stages: the best induction period, half-life period, and residual effect period. A prolonged retention time is unfavorable, and the best induction period should be used.³⁵ Acupuncture analgesia has different optimal times for different diseases, and the analgesic effect of acupuncture gradually reaches saturation as the acupuncture analgesia time extends.³⁶ Acupuncture analgesia requires a 20- to 30-min induction period, after which the analgesic effect of acupuncture gradually weakens, leading to a “tolerance effect”.³⁷ CP/CPPS is characterized by localized pelvic pain.³⁸ Liu et al³⁹ observed that needling the Shiqizhui acupoint for 30 min was more effective than holding the needle for 20 min for relieving pain in patients with primary dysmenorrhea. However, due to the lack of research, the precise duration of needle retention for pain relief remains unknown. To achieve the best therapeutic effect of CP/CPPS, we need to comprehensively analyze the patient’s personal condition, including pain severity, age, physical condition, and post-treatment response, to determine the best retention time of acupuncture.⁴⁰

Course of Treatment

Currently, the dose–response relationship between acupuncture sessions and CP/CPPS outcomes remains unclear, and clinical guidelines for acupuncture do not specify minimum sessions in clinical practice. Four studies^{21,22,27,28} found that the longer the acupuncture session, the more effective it is in lowering NIH-CPSI scores and pain subscores. Zhang et al⁴¹ searched for RCTs that compared the efficacy of acupuncture with that of sham acupuncture or standard medication on CP/CPPS and determined the optimal acupuncture session to achieve clinical efficacy. In the included experiment, the results revealed a dose–response relationship between acupuncture frequency and the therapeutic effect in the case of 6–28 sessions of acupuncture. The overall trend showed that the more acupuncture treatments received, the lower the NIH-CPSI score. According to Zhang et al,⁴¹ four sessions are the minimum “dose” required to achieve clinical efficacy. Therefore, short-term acupuncture treatment may be adequate and effective in some cases, particularly for acute pain. Zhang et al⁴¹ also suggested that acupuncture treatment sessions be extended in cases of refractory CP/CPPS to achieve the best results. Another study by Qin et al⁴² included 10 studies involving 329 participants and found a J-shaped dose–response relationship between acupuncture sessions and the NIH-CPSI score. The NIH-CPSI score decreased from 26.1 (95% CI: 25.3–27.0) to 18.5 (95% CI: 11.6–25.4) after six acupuncture sessions, with a between-session difference of –7.6 (95% CI: –14.6 to –0.7). Considering the 95% CI, both robust-error meta-regression modeling (MD: –8.3 [95% CI: –10.4 to –6.3]) and sensitivity analysis without case series studies (MD: –8.1 [95% CI: –9.5 to –6.7]) demonstrated that the NIH-CPSI score clinically improved after 18 sessions.

Needling Depth

The clinical effect is primarily influenced by the depth of the acupuncture needle. Zhou et al²³ investigated the therapeutic effect of LA on CP/CPPS. In the LA group, the long needle (0.4 × 100 mm) was inserted perpendicularly at BL30 (Baihuanshu) and BL35 (Huiyang) at a depth of 75–90 mm (3–3.5 cun). In the TA group, the same acupoints as those in the LA group were used and a traditional needle (0.3 × 40 mm) was inserted at a depth of 25–35 mm. Both LA and TA reduced the NIH-CPSI scores and pain subscores, but LA had a higher clinical efficacy score. Despite the fact that both shallow and deep punctures are effective in most pain cases, comparative studies on the relationship between acupuncture depth and effect in chronic pelvic pain are lacking. Some studies with large sample sizes have also tentatively shown that the efficacy of deep puncture is similar to that of shallow puncture, although their disease focus was not CP/CPPS.^{43,44} The CP/CPPS acupoints are mostly concentrated in the lumbosacral and buttocks regions (Figure 2). Zhou et al²³ also selected acupoints from these areas. However, it is yet to be determined whether these muscle mass areas are better for treating CP/CPPS.

Evaluation of the Efficacy of TCM

Patients with CP/CPPS not only experience localized pain symptoms, discomfort, and lower-urinary-tract symptoms but also psychological symptoms, insomnia, fatigue, poor appetite, low back pain, and other manifestations, all of which can interfere with recovery. Evaluating the curative effect solely on the basis of the NIH-CPSI score, international prostate symptom score, and other western evaluation standards may be insufficient. In China and other countries, where

acupuncture is popular, researchers are evaluating the efficacy of acupuncture based on the improvement of other concomitant symptoms in patients with CP/CPPS patients, except the pain, to prove the efficacy of acupuncture.

Possible Mechanisms

Acupuncture may reduce pain symptoms by modulating the associated neurotransmitters. The final stage of CP/CPPS may be a neuropathic pain syndrome characterized by chronic pain, recurrent inflammation, voiding disorders, and sexual dysfunction. The pain syndrome can be neurogenically mediated by upregulating the local pelvic/perineal afferent sensory neuronal system and winding it up within the spinal cord and central nervous system, including endogenous opioid system regulation and gating control theories.⁴⁵ The pain-relieving efficacy of acupuncture can be attributed to a complex phenomenon involving numerous neuropeptides and neurotransmitters.⁴⁶ Activation of primary sensory neurons induces the release of inflammatory neuropeptides, such as substance P (SP), which can exacerbate inflammatory cell accumulation. Meanwhile, inflammation and enhanced oxidative stress may activate cyclooxygenase-2 (COX-2), which induces the production of prostaglandin E2 (PGE2) and inhibits the release of β -endorphin (β -EP) secreted by immune cells, resulting in and maintaining CP/CPPS pain symptoms. To alleviate CP/CPPS pain, it is necessary to inhibit PGE2 release while promoting EP accumulation. Acupuncture increases the concentration of β -EP in the cerebrospinal fluid, even in patients with CP/CPPS, as reported by Lee et al⁴⁷ Ma et al⁴⁸ also found that acupuncture burial therapy was better than oral tamsulosin hydrochloride in raising plasma β -EP levels and lowering SP levels in patients with CPPS. Furthermore, acupuncture points in the lumbosacral region and below the umbilicus, such as BL33 (Zhongliao), CV4 (Guanyuan), and CV3 (Zhongji), may cause minor damage to local tissues, allowing endorphins, such as β -EP, and their receptors to accumulate locally for a certain period of time. This phenomenon explains the possible peripheral opioid analgesic effect induced by acupuncture treatment. According to the neurotransmitter theory, acupuncture may also stimulate the release of neurotransmitters, such as serotonin and norepinephrine, as well as regulate dopamine and 5-hydroxytryptamine. However, these mechanisms overlap in some ways, and more experimental data are required to confirm the mechanisms of their roles in the acupuncture treatment of CP/CPPS.^{47,49}

Acupuncture may regulate the effects of inflammatory factors in patients or models with CP/CPPS. COX-2, a key mediator of inflammation, can contribute to the inflammatory response by producing PGE2, which causes local pain and vasodilation. Men with symptomatic CP/CPPS have higher PGE2 concentrations in the prostatic fluid than asymptomatic controls,⁵⁰ implying that the pain in CP/CPPS may be caused by increased prostaglandin production. Hence, methods that lower prostaglandin PGE2 or COX-2 levels within the prostate would be beneficial to men with CP/CPPS. EA therapy is said to be anti-inflammatory because it regulates the expression of proinflammatory cytokines and COX-2 in peripheral and central nociceptive sites.^{51,52} Lee et al²⁷ collected postmassage urine samples and found that the PGE2 levels in the EA group decreased significantly. Furthermore, Jiang et al⁵³ used a rat model of neuropathic pain to investigate the role of PGE2 in EA analgesia. After 7 days of intervention, the expression level of the spinal PGE2 was significantly higher in the model group than in the control group, but it was reversed by EA ($P < 0.01$ and $P < 0.05$). Therefore, EA on neuropathic pain might alleviate the hyperalgesia state by inhibiting the local secretion of PGE2. Furthermore, interleukin-1 β (IL-1 β) and tumor necrosis factor- α (TNF- α) are two important proinflammatory cytokines that may play a role in the development of CP/CPPS.⁵⁴ Alexander et al⁵⁵ observed increased levels of TNF- α and IL-1 β in the seminal plasma of patients with CP. Nadler et al⁵⁶ also reported that TNF- α and IL-1 β levels were significantly higher in the prostatic fluid of patients with CP/CPPS than in the prostatic fluid of healthy controls and that a correlation existed between these cytokines. Furthermore, acupuncture has been shown to have an effect on inflammatory mediators in patients with CP/CPPS, with TNF- α and IL-1 β expression levels being significantly reduced.^{50,57}

Acupuncture may modulate immune responses in patients or models with CP/CPPS. Immune mechanisms, particularly autoreactive T lymphocytes, may play a role in the development of CP/CPPS.^{58,59} T lymphocytes are divided into subsets; CD4+ T cells are helper T lymphocytes that help B lymphocytes produce antibodies and help other T lymphocyte subsets, whereas CD8+ T cells are suppressor and killer T lymphocytes that inhibit lymphocytes from producing antibodies and suppress other lymphocytes.⁶⁰ Natural killer (NK) cells secrete cytokines essential for mediating immune responses; thus, high levels of NK cells may be required in preventing CP/CPPS and other chronic inflammatory conditions.^{61,62} It may also exert positive effects through the production of helper T cell factors associated

with disease remission. Quick et al⁶³ reported that CD4+ T cells play a role in the development of pelvic pain in mice. Ye et al⁶⁴ compared serum immunoglobulin G (IgG) and CD8+ levels in 23 patients with CP/CPPS and 26 healthy people and found that patients with CP/CPPS had lower serum CD8+ levels and higher serum IgG levels than healthy people. Liu et al⁶⁵ investigated the effect of EA on the cellular immune function of rats with chronic nonbacterial prostatitis; results showed that the EA group had significantly higher CD4+ plasma levels and a higher CD4+/CD8+ ratio ($P < 0.01$ and $P < 0.05$), but the difference in CD8+ plasma levels was not statistically significant ($P > 0.05$). Yu et al⁶⁶ demonstrated that 30 min of EA stimulation in ST36 (Zusanli) once a day for 3 days significantly increased splenic NK cell activity in mice. In a clinical study, Lee et al⁶⁷ compared the effects of acupuncture and sham acupuncture on cellular immunity in 12 patients with CP/CPPS. The results showed that 8 (67%) of the participants (four in each group) were classified as treatment responders, and the NK cell level increased by 5% in the acupuncture group compared with that in the sham group (-13% ; $P = 0.03$).

Limitations

In strict accordance with the search strategy of our review, we included 11 English language studies. Because of language barriers, some studies in other languages were excluded. Our study is also limited by a small sample size and poor evidence quality. The purpose of this review was to analyze the usefulness of acupuncture in patients with CP/CPPS from TCM and western medicine perspectives as well as discuss the mechanisms involved. Although the 11 studies mentioned above have consistently demonstrated that acupuncture is effective in lowering NIH-CPSI scores and relieving local pain in patients with CP/CPPS, the underlying mechanisms remain unclear.

Conclusion

This review provides potential evidence and trends for future research to assist clinicians in treating patients with CP/CPPS through acupuncture. According to TCM, the location, retention time, treatment duration, and needling depth affect the efficacy of acupuncture. Based on our findings, we believe that acupoints in the lumbosacral region and bilateral lower extremities are more suitable for the treatment of CP/CPPS during clinical operation, and the locations of these acupoints are mostly located in the bladder meridian of foot-taiyang, ren meridian, and spleen meridian of foot-taiyin, such as those of BL33 (Zhongliao), CV4 (Guanyuan), and SP6 (Sanyinjiao). We also recommend setting the duration of acupuncture treatment for this condition at 20–30 minutes for each session, with at least four sessions. The mechanism of acupuncture for CP/CPPS is mostly attributed to neuromodulatory, immunomodulatory, and anti-inflammatory functions. We suggest that future studies should focus on the application of acupoints, as well as a more standard design in terms of the course, retention time, and frequency. And ultimately, a clinical protocol for the treatment of CP/CPPS with acupuncture will be developed. On this basis, the further validation of the mechanism in acupuncture for CP/CPPS is still necessary.

Data Sharing Statement

Data supporting this article are all in this article.

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Disclosure

The authors report no conflicts of interest in this work.

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