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Efficacy of Acupuncture for Chronic Prostatitis/Chronic Pelvic Pain Syndrome

A Randomized Trial

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Background: Acupuncture has promising effects on chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS), but high-quality evidence is scarce.

Objective: To assess the long-term efficacy of acupuncture for CP/CPPS.

Design: Multicenter, randomized, sham-controlled trial. (Clinical Trials.gov: NCT03213938)

Setting: Ten tertiary hospitals in China.

Participants: Men with moderate to severe CP/CPPS, regardless of prior exposure to acupuncture.

Intervention: Twenty sessions of acupuncture or sham acupuncture over 8 weeks, with 24-week follow-up after treatment.

Measurements: The primary outcome was the proportion of responders, defined as participants who achieved a clinically important reduction of at least 6 points from baseline on the National Institutes of Health Chronic Prostatitis Symptom Index at weeks 8 and 32. Ascertainment of sustained efficacy required the between-group difference to be statistically significant at both time points.

Results: A total of 440 men (220 in each group) were recruited. At week 8, the proportions of responders were 60.6% (95% CI, 53.7% to 67.1%) in the acupuncture group and 36.8% (CI, 30.4% to 43.7%) in the sham acupuncture group (adjusted difference, 21.6 percentage points [CI, 12.8 to 30.4 percentage points]; adjusted odds ratio, 2.6 [CI, 1.8 to 4.0]; $P < 0.001$). At week 32, the proportions were 61.5% (CI, 54.5% to 68.1%) in the acupuncture group and 38.3% (CI, 31.7% to 45.4%) in the sham acupuncture group (adjusted difference, 21.1 percentage points [CI, 12.2 to 30.1 percentage points]; adjusted odds ratio, 2.6 [CI, 1.7 to 3.9]; $P < 0.001$). Twenty (9.1%) and 14 (6.4%) adverse events were reported in the acupuncture and sham acupuncture groups, respectively. No serious adverse events were reported.

Limitation: Sham acupuncture might have had certain physiologic effects.

Conclusion: Compared with sham therapy, 20 sessions of acupuncture over 8 weeks resulted in greater improvement in symptoms of moderate to severe CP/CPPS, with durable effects 24 weeks after treatment.

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Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) involves urogenital pain, lower urinary tract symptoms, psychological issues, and sexual dysfunction (1). It affects 2% to 16% of the population in high-income countries and 11% in low- and middle-income countries (2, 3). The negative effect of CP/CPPS on quality of life is similar to that of angina, myocardial infarction, congestive heart failure, diabetes mellitus, and Crohn disease (4, 5). Its pathophysiology may involve a composite of neuropsychophysiologic factors, such as inflammation in the prostate, anxiety and stress, and dyssynergic voiding (6, 7). Although empirical antibiotics, α-blockers, and anti-inflammatories are the mainstays of treatment in clinical practice, they often target only 1 aspect of the disease and have not shown beneficial effects compared with placebo (8–10). In addition, relief of CP/CPPS is limited to the period of medication use, and efficacy tends to fade after medication use is discontinued; an increased incidence of adverse events has to be taken into account with long-term use (11–13).

Acupuncture has long been a nonpharmaceutical choice for pain management, with sustained effects over 12 months (14), and pelvic pain is among the most common indications (15). In a recent Cochrane review on CP/CPPS that assessed 20 nonpharmacologic interventions, only acupuncture and extracorporeal shockwave therapy were likely to result in symptom relief with a good safety profile (16). However, a clinically meaningful responder analysis found that acupuncture resulted in little or no difference compared with sham acupuncture in the number of persons who achieved the minimal

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clinically important difference of 6 points on the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), although the quality of the evidence was very low (16). In addition, the durability of acupuncture effects is still not clear (7, 17).

Our pilot study revealed that a significantly larger number of persons with CP/CPPS who received 8 weeks of acupuncture had positive outcomes 24 weeks after treatment compared with those receiving sham acupuncture, suggesting clinically meaningful and potentially long-lasting benefits of acupuncture for CP/CPPS (18). We therefore conducted this multicenter, large-scale, randomized trial to assess the long-term efficacy of acupuncture for CP/CPPS.

METHODS

Design Overview

This was a 10-center, randomized, sham-controlled trial involving men with CP/CPPS. The study was approved by the institutional review boards at the coordinating center and each study site (**Supplement 1**, available at Annals.org). The protocol (**Supplement 2**, available at Annals.org) has been published previously (19). All participants provided informed consent.

Setting and Participants

The study was conducted in the outpatient departments of 10 tertiary hospitals in cities across China. Volunteers were recruited via newspapers, a website, and hospital posters. The diagnosis of CP/CPPS was made by urologists using medical history, physical examinations, and laboratory tests; a 2-glass test (20) was performed in every participant to collect urine specimens and expressed prostatic secretion for analysis and culture. Men were eligible if they had experienced discomfort or pain in the pelvic region for at least 3 of the previous 6 months without evidence of infection (21), were aged 18 to 50 years, and reported a total score of at least 15 on the NIH-CPSI.

We excluded men with other types of prostatitis; urogenital infection; history of genitourinary cancer; bladder outlet obstruction; overactive bladder; interstitial cystitis; neurogenic bladder; postvoid residual urine volume of 100 mL or greater; maximum flow rate of 15 mL/s or less; inflammatory bowel disease; neurologic impairment affecting the bladder; psychiatric disorder; severe cardiac, respiratory, or hematopoietic disorders; liver or renal dysfunction; or medical therapy for CP/CPPS in the previous 4 weeks. Participants with prior exposure to acupuncture were not excluded.

Randomization and Masking

Eligible participants were randomly assigned in a 1:1 ratio to acupuncture or sham acupuncture via the web-response system of the Central Randomization System for Clinical Research. The randomization was performed with permuted blocks of size 4 or 6, stratified according to site. Participants, outcome assessors, and statisticians were blinded to treatment assignment, but acupuncturists were not.

Interventions

The intervention protocol was based on our pilot study (18) and expert consensus. The treatments were administered by certified acupuncturists (≥2 at each site) who had 5 years of undergraduate education on acupuncture and at least 2 years of clinical experience.

For the acupuncture group, acupoints of bilateral Zhongliao (BL33), Huiyang (BL35), Shenshu (BL23), and Sanyinjiao (SP6) were used (**Figure 1** of **Supplement 3**, available at Annals.org). Stainless steel, single-use, sterile needles were inserted to a depth of 50 to 60 mm at BL33 (at an angle of 30° to 45° in an inferomedial direction) and BL35 (in a slightly superolateral direction); at BL23 and SP6, the needles were inserted vertically to a depth of 25 to 30 mm. After needle insertion, gentle and even manipulations (once every 10 minutes, 30 seconds each time) involving lifting, thrusting, twirling, and rotating were performed at all acupoints except BL33 to attain deqi (a sensation of aching, soreness, swelling, heaviness, or numbness [22]). For the sham acupuncture group, minimally invasive needles were inserted to a depth of 2 to 3 mm at bilateral nonacupoints (15 mm lateral to BL23, BL33, and BL35 and 10 mm lateral to SP6 [**Figure 1** of **Supplement 3**]) without manipulation.

Participants in both groups started treatment on the day of randomization and received twenty 30-minute sessions over 8 consecutive weeks: 3 sessions in each of the first 4 weeks (ideally every other day) followed by 2 sessions per week (ideally every 2 or 3 days) in the remaining 4 weeks. All participants were followed for 24 weeks after treatment.

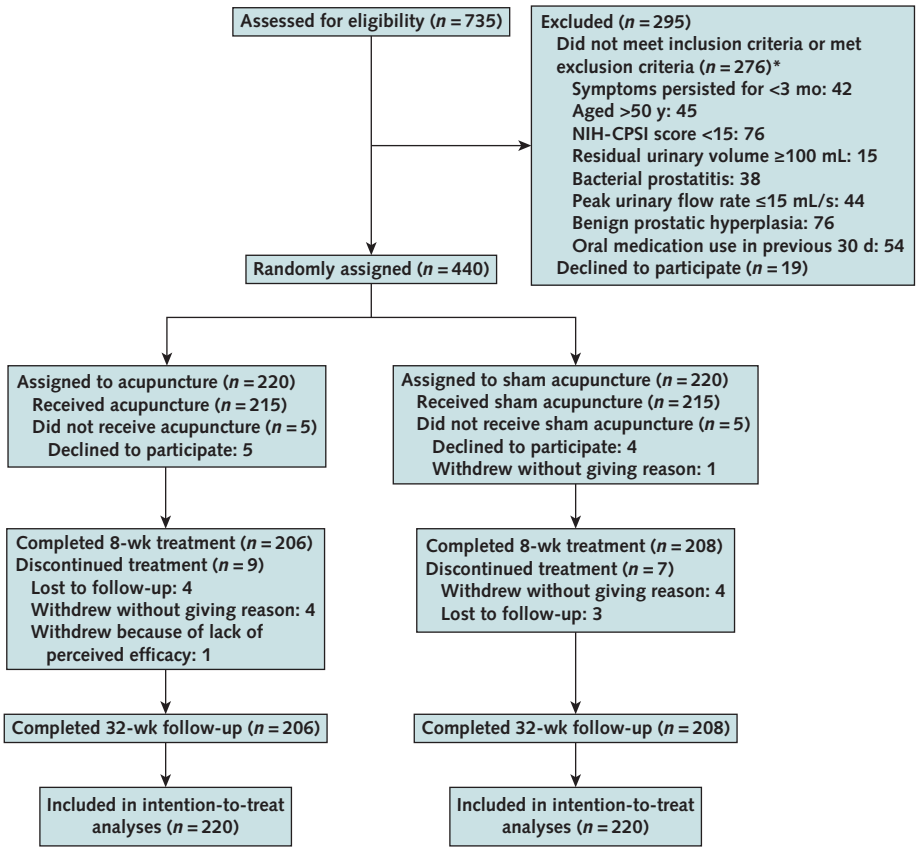
A total of 23 acupuncturists administered the treatment. They could perform both acupuncture and sham acupuncture, with priority given to the same acupuncturist delivering treatment to a specific participant throughout the trial whenever possible. Acupuncturists were not allowed to disclose group allocation to participants and conducted the treatment in accordance with standardized operating procedures across groups (**Supplement 2**). Before treatment, participants were told they would receive either traditional acupuncture with relatively deep needle insertion or minimal acupuncture with relatively shallow insertion at nonacupoints. Participants were treated by appointment to maintain blinding and avoid communication. The acupoints that were used are located in the lumbosacral and posterior tibial regions and were difficult for participants to see while prone. Participants might sense the needle piercing the skin but usually were unable to tell how deeply it was inserted. To test the success of blinding, within 5 minutes after either treatment session at week 8, participants were asked whether they had received traditional acupuncture in the previous weeks (yes, no, or unclear).

Participants were encouraged to refrain from using medications or other therapies for management of CP/CPPS throughout the trial. If other therapies were used, details were documented on a concomitant medications form.

Assessments and Outcomes

The primary outcome was the proportion of responders, defined as those with a reduction of at least 6 points from baseline in the NIH-CPSI total score. The NIH-CPSI was administered at weeks 1 to 8, 20, and 32.

Figure 1. Study flow diagram.



NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index.
* Some participants had >1 reason for exclusion.

Response was assessed immediately after the 8-week treatment (week 8) and 24 weeks after treatment (week 32); the between-group difference had to be statistically significant at both time points for us to conclude efficacy for at least 24 weeks.

The NIH-CPSI is a universally accepted, reliable, and valid instrument recommended by consensus guidelines for clinical evaluation of and research on CP/CPPS (1, 23). It measures pain (score range, 0 to 21), urinary function (score range, 0 to 10), and effect on quality of life (score range, 0 to 12), with a total score ranging from 0 to 43 and higher scores indicating worse conditions (23). A 6-point decrease in the total score was identified by receiver-operating characteristic curve as the optimal threshold, with high sensitivity, specificity, and discriminative ability to differentiate clinically important improvement. The NIH-CPSI correlated well with the global response assessment (GRA) (a 7-point assessment on participant-perceived improvement with treatment), which has been used in clinical trials to designate participants reporting marked or moderate improvement as clinical responders (24).

The GRA and the Chinese-version International Index of Erectile Function 5 (IIEF-5) were administered at weeks 4, 8, 20, and 32. The International Prostate Symptom Score (IPSS), the Hospital Anxiety and Depression Scale (HADS), and the EuroQol 5 Dimension 5 Level (EQ-5D-5L) were administered at weeks 8, 20, and 32. The IIEF-5 score ranges from 0 to 25, with lower scores indicating more severe dysfunction; the minimal clinically important difference is 5 points (25, 26). The IPSS ranges from 0 to 35, with higher scores indicating more severe urinary symptoms (27). The HADS score ranges from 0 to 42, with higher scores indicating greater anxiety and depression (28). The EQ-5D-5L overall index ranges from −0.39 to 1.00 (29), with a higher overall index indicating better generic health status (30). Peak and average urinary flow rates were assessed at weeks 8 and 32.

Participants' expectations of acupuncture for general illness and for CP/CPPS were assessed before treatment. Blinding was assessed using the James and Bang blinding indices (31). Adherence was assessed by counting the number of treatment sessions.

Adverse events were documented by participants and outcome assessors on a form throughout the trial. All adverse events were systematically collected via semi-structured and open-ended questions and were categorized by acupuncturists and urologists as treatment-related or non–treatment-related within 24 hours of

Table 1. Baseline Characteristics of the Study Population*

Characteristic	Acupuncture (*n* = 220)†	Sham Acupuncture (*n* = 220)†
Mean age (SD), *y*	35.5 (8.0)	36.1 (7.9)
Race, *n (%)*‡		
Han	213 (99.1)	214 (99.1)
Other	2 (0.9)	2 (1.0)
Mean body mass index (SD), kg/m^2	23.6 (3.1)	24.3 (7.4)
Married, *n (%)*	152 (71.4)	165 (76.4)
Median sexual frequency per week (range)	1.0 (1.0 to 2.0)	1.0 (1.0 to 2.0)
Education level, *n (%)*		
Primary education or less	2 (0.9)	1 (0.5)
Secondary education	98 (46.4)	95 (44.0)
Tertiary education	111 (52.6)	120 (55.6)
Current smoker, *n (%)*	79 (37.1)	71 (32.9)
Current drinker, *n (%)*	112 (53.1)	112 (52.3)
Eating preferences, *n (%)*		
Normal	160 (76.6)	160 (74.4)
Fast food	7 (3.3)	12 (5.6)
Light	21 (10.0)	23 (10.7)
Spicy	14 (6.7)	15 (7.0)
Tea/coffee	7 (3.3)	5 (2.3)
Habit of staying up late, *n (%)*	120 (56.3)	99 (46.0)
Sedentary lifestyle, *n (%)*	147 (70.3)	148 (69.5)
Median CP/CPPS symptom duration (range), *y*	2 (1.0 to 4.0)	2 (1 to 3.5)
Comorbidities, *n (%)*	11 (5.1)	11 (5.1)
Neck, waist, or knee pain	3 (1.4)	2 (0.9)
Chronic gastritis	2 (0.9)	3 (1.4)
Anxiety and insomnia	1 (0.5)	3 (1.4)
Benign prostatic hyperplasia	2 (0.9)	2 (0.9)
Other	5 (2.3)	2 (0.9)
Previous treatments for CP/CPPS, *n (%)*	99 (46.0)	102 (47.4)
Herbal medicine	77 (35.8)	74 (33.4)
Local treatments	21 (9.8)	25 (11.6)
Antibiotics	17 (7.9)	18 (8.4)
α-Blockers	8 (3.7)	13 (6.0)
Acupuncture	3 (1.4)	10 (4.7)
Physical therapy	5 (2.3)	6 (2.8)
5-α-Reductase inhibitors	5 (2.3)	2 (0.9)
Other	10 (4.7)	10 (4.7)
Mean NIH-CPSI score (SD)§		
Total (range, 0 to 43)	31.0 (4.8)	31.4 (5.2)
Pain subscale (range, 0 to 21)	16.4 (2.6)	16.6 (2.8)
Urinary subscale (range, 0 to 10)	5.3 (2.6)	5.5 (2.6)
Quality-of-life subscale (range, 0 to 12)	9.3 (2.0)	9.3 (2.0)
Mean IPSS score (SD) (range, 0 to 35)§	11.3 (6.4)	12.2 (6.8)
Mean IIEF-5 score (SD) (range, 0 to 25)‖	15.1 (5.7)	15.4 (5.6)
Mean HADS score (SD) (range, 0 to 42)§	13.6 (6.9)	13.6 (6.6)
Mean EQ-5D-5L overall index (SD) (range, −0.39 to 1.00)¶	0.8 (0.1)	0.9 (0.1)
Mean peak urinary flow rate (SD), *mL/s*	22.0 (7.4)	21.7 (6.2)
Mean average urinary flow rate (SD), *mL/s*	12.5 (5.1)	11.9 (3.9)
Median total prostate-specific antigen level (range), *ng/mL*	0.6 (0.3 to 1.1)	0.6 (0.3 to 1.2)
Median residual urinary volume (range), *mL*	4.5 (0 to 14.0)	4.0 (0 to 15.0)

CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; EQ-5D-5L = EuroQol 5 Dimension 5 Level; HADS = Hospital Anxiety and Depression Scale; IIEF-5 = International Index of Erectile Function 5; IPSS = International Prostate Symptom Score; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index.

* Ten participants (5 [who declined to participate] in the acupuncture group and 5 [4 who declined to participate and 1 who withdrew without giving a reason] in the sham acupuncture group) did not receive the study treatment.

† Sample sizes for individual characteristics varied because of missing data (*n* = 203 to 220 in the acupuncture group and 211 to 220 in the sham acupuncture group).

‡ Self-reported by participants.

§ Higher scores on the NIH-CPSI, IPSS, and HADS indicate worse symptoms.

‖ Higher scores on the IIEF-5 indicate better sexual function.

¶ Higher EQ-5D-5L overall index indicates better health.

occurrence. Discrepancies were resolved via discussion and consensus. Serious adverse events were immediately reported to the principal investigator (Z.L.) and were reported to the institutional review board at the coordinating center and the clinical sites within 24 hours. All adverse events were followed up until resolution.

Statistical Analysis

On the basis of previously published data in similar populations (18), we anticipated a 46.7% responder rate in the sham acupuncture group. A sample size of 440 participants was estimated to provide 90% power to detect a between-group difference of 17 percentage points (63.7% vs. 46.7%;

Table 2. Primary and Secondary Outcomes

Outcome	Acupuncture (*n* = 220)	Sham Acupuncture (*n* = 220)	Adjusted Odds Ratio or Adjusted Difference (95% CI)
Primary outcome*			
Responders (95% CI), %			
Week 8	60.6 (53.7 to 67.1)	36.8 (30.4 to 43.7)	2.6 (1.8 to 4.0)†
Week 32	61.5 (54.5 to 68.1)	38.3 (31.7 to 45.4)	2.6 (1.7 to 3.9)†
Secondary outcomes			
Adjusted mean change in NIH-CPSI total score (95% CI)‡			
Week 4	−4.8 (−5.4 to −4.3)	−3.7 (−4.2 to −3.1)	−1.2 (−1.9 to −0.4)
Week 8	−7.4 (−8.0 to −6.8)	−4.9 (−5.5 to −4.3)	−2.5 (−3.4 to −1.6)
Week 20	−7.2 (−8.0 to −6.6)	−4.5 (−5.2 to −3.9)	−2.7 (−3.7 to −1.8)
Week 32	−7.4 (−8.1 to −6.7)	−4.9 (−5.5 to −4.2)	−2.6 (−3.5 to −1.6)
Adjusted mean change in NIH-CPSI pain subscale score (95% CI)‡			
Week 4	−1.6 (−1.8 to −1.3)	−1.1 (−1.3 to −0.9)	−0.5 (−0.8 to −0.1)
Week 8	−2.1 (−2.4 to −1.9)	−1.3 (−1.5 to −1.1)	−0.8 (−1.2 to −0.5)
Week 20	−2.0 (−2.3 to −1.8)	−1.0 (−1.2 to −0.7)	−1.0 (−1.4 to −0.7)
Week 32	−2.0 (−2.3 to −1.8)	−1.3 (−1.5 to −1.0)	−0.8 (−1.1 to −0.4)
Adjusted mean change in NIH-CPSI urinary subscale score (95% CI)‡			
Week 4	−1.3 (−1.6 to −1.1)	−1.0 (−1.2 to −0.8)	−0.3 (−0.6 to 0)
Week 8	−2.1 (−2.4 to −1.9)	−1.4 (−1.6 to −1.2)	−0.7 (−1.1 to −0.4)
Week 20	−2.1 (−2.3 to −1.8)	−1.5 (−1.7 to −1.2)	−0.6 (−1.0 to −0.2)
Week 32	−2.1 (−2.4 to −1.9)	−1.5 (−1.8 to −1.2)	−0.6 (−1.0 to −0.3)
Adjusted mean change in NIH-CPSI quality-of-life subscale score (95% CI)‡			
Week 4	−1.9 (−2.2 to −1.7)	−1.5 (−1.8 to −1.3)	−0.4 (−0.8 to 0)
Week 8	−3.1 (−3.4 to −2.8)	−2.2 (−2.4 to −1.9)	−0.9 (−1.4 to −0.5)
Week 20	−3.2 (−3.5 to −2.8)	−2.0 (−2.4 to −1.7)	−1.1 (−1.6 to −0.6)
Week 32	−3.1 (−3.5 to −2.8)	−2.1 (−2.4 to −1.8)	−1.1 (−1.5 to −0.6)
Adjusted mean change in IPSS score (95% CI)‡			
Week 4	−2.7 (−3.2 to −2.3)	−1.7 (−2.1 to −1.2)	−1.1 (−1.8 to −0.4)
Week 8	−4.4 (−4.9 to −3.9)	−2.7 (−3.2 to −2.2)	−1.7 (−2.5 to −0.9)
Week 20	−4.7 (−5.3 to −4.2)	−3.0 (−3.6 to −2.4)	−1.8 (−2.6 to −0.9)
Week 32	−4.7 (−5.4 to −4.1)	−3.1 (−3.8 to −2.5)	−1.6 (−2.5 to −0.8)
Adjusted mean change in IIEF-5 score (95% CI)§			
Week 8	0.8 (0.2 to 1.3)	0.3 (−0.3 to 0.8)	0.5 (−0.3 to 1.2)
Week 20	0.7 (0.2 to 1.3)	0.2 (−0.3 to 0.7)	0.5 (−0.2 to 1.3)
Week 32	1.0 (0.4 to 1.6)	0.4 (−0.1 to 1.0)	0.6 (−0.3 to 1.4)
Adjusted mean change in HADS score (95% CI)‡			
Week 8	−1.9 (−2.5 to −1.4)	−0.8 (−1.3 to −0.3)	−1.1 (−1.9 to −0.4)
Week 20	−2.4 (−3.0 to −1.8)	−0.6 (−1.3 to 0)	−1.7 (−2.6 to −0.9)
Week 32	−2.8 (−3.5 to −2.2)	−0.5 (−1.2 to 0.1)	−2.3 (−3.2 to −1.4)
Adjusted mean change in EQ-5D-5L score (95% CI)§			
Week 8	0.06 (0.05 to 0.07)	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.04)
Week 20	0.06 (0.05 to 0.07)	0.03 (0.02 to 0.04)	0.03 (0.02 to 0.05)
Week 32	0.06 (0.05 to 0.08)	0.03 (0.02 to 0.04)	0.04 (0.02 to 0.05)
Adjusted mean change in peak urinary flow rate (95% CI), *mL/s*§			
Week 8	0.6 (−0.3 to 1.6)	0.7 (−0.2 to 1.6)	−0.1 (−1.4 to 1.3)
Week 32	0.5 (−0.4 to 1.3)	−0.6 (−1.4 to 0.2)	1.1 (−0.1 to 2.2)
Adjusted mean change in average urinary flow rate (95% CI), *mL/s*§			
Week 8	0.6 (0.1 to 1.1)	0.4 (−0.1 to 0.9)	0.2 (−0.5 to 0.9)
Week 32	0.5 (0.1 to 1.0)	−0.2 (−0.6 to 0.3)	0.7 (0 to 1.3)
Use of other treatment for CP/CPPS during study, *n (%)*‖	16 (7.4)	15 (7.0)	NA
Herbal medicine	9 (4.2)	5 (2.3)	NA
Antibiotics	5 (2.3)	7 (3.3)	NA

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Table2–Continued

Outcome	Acupuncture (*n* = 220)	Sham Acupuncture (*n* = 220)	Adjusted Odds Ratio or Adjusted Difference (95% CI)
Infrared therapy or moxibustion	4 (1.9)	3 (1.4)	NA
α-Blockers or 5-α-reductase inhibitors	3 (1.4)	1 (0.5)	NA
Hip bath	1 (0.5)	1 (0.5)	NA
Sertraline	0	1 (0.5)	NA

CP/CPPS = chronic prostatitis/chronic pelvic pain syndrome; EQ-5D-5L = EuroQol 5 Dimension 5 Level; HADS = Hospital Anxiety and Depression Scale; IIEF-5 = International Index of Erectile Function 5; IPSS = International Prostate Symptom Score; NA = not applicable; NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index.

* Defined as a reduction of ≥6 points from baseline in the NIH-CPSI total score. Details on the responder analyses at each visit are provided in Figure 2 and in Table 7 of Supplement 3 (available at Annals.org).

† Odds ratios are from the prespecified logistic generalized linear mixed model and are adjusted for baseline NIH-CPSI total score.

‡ Negative changes indicate better outcomes. Data were calculated using a mixed-effects model with baseline adjustment.

§ Positive changes indicate better outcomes. Data were calculated using a mixed-effects model with baseline adjustment.

‖ Ten participants (5 [who declined to participate] in the acupuncture group and 5 [4 who declined to participate and 1 who withdrew without giving a reason] in the sham acupuncture group) did not receive the study treatment. Data were reported for descriptive purposes only; thus, differences between groups are not provided.

odds ratio, 2.0) at a 2-sided significance level of 5%. This proposed sample size included a 15% increase to account for dropouts.

The primary outcome was assessed by fitting a logistic generalized linear mixed model for repeated measures (SAS PROC GLIMMIX). Response or nonresponse at each scheduled postbaseline visit was the dependent variable. According to the prespecified protocol (19), participants who withdrew from the study without an NIH-CPSI score were considered nonresponders. The logistic generalized linear mixed model included the baseline NIH-CPSI total score as a covariate, with treatment group (acupuncture or sham acupuncture), visit, and treatment-by-visit interaction as fixed effects. Between-group comparisons at each visit were estimated by differences between least-squares means from the treatment-by-visit interaction and are presented as odds ratios with accompanying *P* values and 95% CIs. The predicted probability of response at each visit is also presented. An unstructured covariance pattern was used to estimate the variance–covariance of the within-subject repeated measures. To control for type I error, the 2 time points had to be positive in order for the trial to prove the durable efficacy of acupuncture. In addition, to estimate the risk difference between groups for the primary outcome, a post hoc analysis was performed using a generalized linear model with a binomial distribution and identity link (SAS PROC GENMOD) that included the same covariate as the logistic generalized linear mixed model.

The changes from baseline in the NIH-CPSI total score were analyzed by fitting linear mixed-effects models using the baseline value as a covariate and treatment, visit, and treatment-by-visit interaction as fixed effects (SAS PROC MIXED). The same approach was used for other continuous variables, such as the HADS score and the IPSS. Participants' expectations of acupuncture for general illness and for CP/CPPS, adherence, and adverse event data were provided for descriptive purposes only. The James and Bang indices were used to evaluate the success of blinding (32).

To assess the robustness of the primary analyses, 3 sensitivity analyses were performed. First, multiple imputation under the missing-at-random assumption was used to generate 100 imputed data sets for missing baseline NIH-CPSI total score and response data (SAS PROC MI). Second, data from participants who responded that they received sham acupuncture during the blinding assessment were excluded. Third, the acupuncturist variable was added as a random effect to account for clustering by acupuncturists. Details are provided in Supplement 3.

All statistical analyses were performed according to the intention-to-treat principle using SAS, version 9.4 (SAS Institute), or Stata, version 15.1 (StataCorp), with a 2-sided *P* value less than 0.05 considered significant. No adjustment was made for multiple comparisons; therefore, secondary outcomes should be interpreted as exploratory. Details on the statistical analyses are provided in Supplement 3.

Role of the Funding Source

The funders of the study had no role in the study design; collection, analysis, or interpretation of the data; or writing of the report.

RESULTS

A total of 735 men were screened for eligibility between October 2017 and April 2019, of whom 440 were randomly assigned to acupuncture or sham acupuncture and 414 (94.1%) completed the trial (Figure 1). Baseline characteristics were similar between groups (Table 1). The mean age of the included participants was 35.8 years (SD, 7.9), and the median duration of CP/CPPS symptoms was 2.0 years (range, 1.0 to 3.8 years).

Participants' expectations of acupuncture were similar in both groups at baseline (Table 1 of Supplement 3). The 26 participants who withdrew without an NIH-CPSI score were considered nonresponders in the intention-to-treat analysis. In the blinding assessment, 1 (0.5%) participant in the acupuncture group and 13 (6.3%) in the sham acupuncture group perceived that they had received sham acupuncture at week 8 (Table 2 of Supplement 3). The mean number of treatment sessions was 18.9 (SD, 3.9) in the acupuncture group and 19.1 (SD, 3.5) in the sham acupuncture group; 94.1% of participants in the acupuncture group and 94.6% in the sham acupuncture group

attended at least 16 (≥80%) sessions (Table 3 of Supplement 3).

At week 8, the proportions of responders were 60.6% (95% CI, 53.7% to 67.1%) in the acupuncture group versus 36.8% (CI, 30.4% to 43.7%) in the sham acupuncture group (adjusted difference, 21.6 percentage points [CI, 12.8 to 30.4 percentage points]; adjusted odds ratio, 2.6 [CI, 1.8 to 4.0]; $P < 0.001$) (Table 2). At week 32, the proportions of responders were 61.5% (CI, 54.5% to 68.1%) in the acupuncture group versus 38.3% (CI, 31.7% to 45.4%) in the sham acupuncture group (adjusted difference, 21.1 percentage points [CI, 12.2 to 30.1 percentage points]; adjusted odds ratio, 2.6 [CI, 1.7 to 3.9]; $P < 0.001$) (Table 2). Sensitivity analyses showed similar results (Tables 4 to 6 of Supplement 3). The between-group difference in the proportion of responders increased gradually during the 8-week treatment, became notable around week 4, and was maintained during the 24-week follow-up after treatment (Figure 2, *top*; Table 7 of Supplement 3).

The average decrease from baseline in the NIH-CPSI total score exceeded 6 points at week 7 and persisted through week 32 in the acupuncture group but was under 6 points throughout the 32 weeks in the sham acupuncture group (Figure 2, *bottom*; Table 7 of Supplement 3). The average change from baseline in the total score was apparently higher in the acupuncture group than the sham acupuncture group starting at week 3, with between-group differences of −2.5 (CI, −3.4 to −1.6) at week 8 and −2.6 (CI, −3.5 to −1.6) at week 32 (Table 2). The between-group differences in the average change from baseline in the NIH-CPSI total and subscale scores followed similar trends of decreasing over the treatment period and stabilizing during follow-up (Figure 2, *bottom*; Figure 2 and Table 7 of Supplement 3).

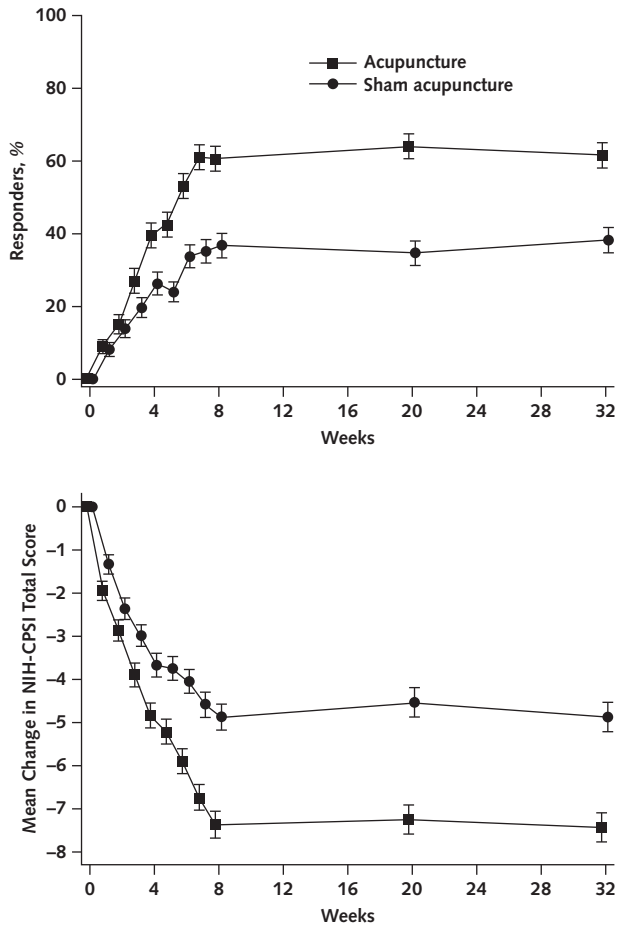
Compared with the sham acupuncture group, larger proportions of participants in the acupuncture group reported marked or moderate improvements on the GRA at all assessment points (Table 8 of Supplement 3). Participants in the acupuncture group had greater decreases in the IPSS and HADS scores (indicating greater symptom improvement) and greater increases in the EQ-5D-5L overall index (indicating better efficacy) for all assessments (Table 2). No significant difference was found in changes in IIEF-5 score at all assessment time points or in peak and average urinary flow rates at week 8 (Table 2). In both groups, similarly small proportions (<5%) of participants used other treatments for CP/CPPS (Table 2).

Twenty (9.1%) adverse events occurred in the acupuncture group, and 14 (6.4%) occurred in the sham acupuncture group. Treatment-related adverse events were mild and transient. No serious adverse events were reported in either group (Table 3).

DISCUSSION

This multicenter randomized trial showed that, compared with sham acupuncture, 20 sessions of acupuncture over 8 weeks provided clinical relief of symptoms of moderate to severe CP/CPPS in a substantially higher proportion of participants, although the net between-group difference in the NIH-CPSI score was modest.

Figure 2. Response on the NIH-CPSI over time.



Error bars represent 95% CIs. NIH-CPSI = National Institutes of Health Chronic Prostatitis Symptom Index. **Top.** Proportion of participants with a reduction of ≥6 points in the NIH-CPSI total score from baseline. **Bottom.** Mean change in NIH-CPSI total score from baseline.

Efficacy may last 24 weeks after treatment. Acupuncture also improved associated symptoms of pain, voiding dysfunction, anxiety, and depression as well as quality of life but not sexual dysfunction compared with sham acupuncture. Both acupuncture and sham acupuncture were safe.

Findings of 3 clinical trials, all conducted in accordance with NIH consensus criteria, suggested that electroacupuncture or acupuncture was more effective than a sham procedure for CP/CPPS. Lee and Lee (33) evaluated the efficacy of electroacupuncture as add-on therapy to advice and exercise in 39 participants, with no additional follow-up after 6 weeks of treatment. Sahin (34) and Lee (35) and their respective colleagues found that acupuncture greatly relieved CP/CPPS symptoms, and the effects lasted through 24 weeks of follow-up among 100 and 90 participants, respectively; however, Sahin and colleagues (34) used a 50% reduction in the NIH-CPSI total score in responder analyses rather than a 6-point reduction. In addition, the long-term response was interpreted as exploratory in both trials, precluding

Table 3. Adverse Events Related and Unrelated to Treatment*

Adverse Event	Acupuncture (*n* = 220)	Sham Acupuncture (*n* = 220)
Any	20 (9.1)	14 (6.4)†
Serious	0	0
Related to treatment‡		
Subcutaneous hematoma	9 (4.1)	5 (2.3)
Localized infection	1 (0.5)	0
Nausea	1 (0.5)	0
Unrelated to treatment		
Cold	7 (3.2)	6 (2.7)
Fever	1 (0.5)	1 (0.5)
Tonsillitis	0	1 (0.5)
Fall	0	1 (0.5)
Pneumonia	1 (0.5)	0
Acute gastritis	0	1 (0.5)

* Data are numbers (percentages).
† Adverse events were counted by type rather than frequency in the same participant. Adverse events of different types occurring in a single participant were defined as independent adverse events. An adverse event with multiple occurrences in a single participant was defined as 1 adverse event.
‡ A treatment-related adverse event was defined as any adverse event that was considered to be possibly, probably, or definitely related to the trial intervention as determined by acupuncturists and urologists. The urologists were unaware of treatment group assignments. Treatment-related adverse events were mild and transient.

a solid conclusion of durability (17). Results of these trials might be biased to varying degrees because all of them were conducted in a single site with a small sample; prognosis factors (drinking, smoking, staying up late, and sedentariness) were unclear at baseline; and the influence of participant expectation and the success of blinding were not assessed, except by Lee and colleagues (35). Our multicenter trial with 440 participants adds evidence on the efficacy of acupuncture for CP/CPPS and may fill the gap in knowledge about durability referenced by the European Association of Urology recommendations (7).

It is intriguing that the results of the responder analyses did not correlate with overall symptom improvement based on mean symptom scores. The between-group differences in the mean NIH-CPSI total score were both less than 6 points (2.5 at week 8 and 2.6 at week 32), although the net changes from baseline were more than 7 points in the acupuncture group but less than 5 points in the sham acupuncture group at weeks 8 and 32. This discrepancy between surprisingly obvious responses and dismal overall differences in mean symptom scores was also found in a pharmaceutical trial of CP/CPPS (36), which indicated that some participants with CP/CPPS probably responded more favorably to the intervention than others. This discrepancy also suggests a substantial placebo effect of acupuncture on CP/CPPS. The decrease from baseline in the NIH-CPSI total score was 4.9 both after treatment and during follow-up in our sham acupuncture group, which exceeds the threshold of 4 points used as the minimal clinically important difference in some early-phase trials (8, 9). This is consistent with previous studies that found that sham acupuncture itself was associated with larger effects than analgesics for chronic pain (37, 38). However, acupuncture is a complex therapy, and placebo effects are inherent in its overall therapeutic effects because of an intimate interaction among the patient, the clinician, and the treatment environment (39, 40). In addition, although the sham procedure using superficial needling at nonacupoints has been proved to be valid in assessing the efficacy of acupuncture on CP/CPPS (41), it may still have physiologic effects and thus decrease the difference between groups (42, 43).

Acupuncture may relieve CP/CPPS symptoms via several mechanisms. Acupuncture is a complex intervention that combines neurophysiologic stimulation from needling with interaction between the clinician and patient. Stimulation at acupoints can promote the release of central opioid peptides (enkephalins, endorphins, and dynorphins) into the blood, which produces analgesic effects and induces a feeling of euphoria (44). Acupuncture can generate anti-inflammatory effects by inhibiting cyclooxygenase synthesis in peripheral and central nociceptive sites (45). For example, it can decrease levels of prostaglandin E2, which is highly expressed in patients with CP/CPPS and is widely recognized to mediate inflammation and pain perception (33, 46). In addition, benefits of effective clinician–patient interaction are far-reaching and well documented, and this is probably also true of acupuncture for CP/CPPS, especially because the condition causes a heavy psychosocial burden (47). Nonetheless, the exact underlying mechanisms of acupuncture for CP/CPPS warrant further investigation.

This trial has limitations. First, sham acupuncture might have produced certain physiologic effects. Second, participants were relatively young but had moderate to severe CP/CPPS; this along with other demographic characteristics may limit the generalizability of the findings to clinical practice. Third, prior acupuncture exposure might have confounded the results, even though blinding assessment and sensitivity analysis confirmed its influence to be minimal. Finally, the protocol of 20 acupuncture sessions over 8 weeks might be a burden to patients in other countries.

In conclusion, 8 weeks of acupuncture may result in clinically important improvements in symptoms of moderate to severe CP/CPPS, with durable efficacy for at least 24 weeks after treatment. This trial showed long-term efficacy of acupuncture and provides high-quality evidence for clinical practice and guideline recommendations. Future research is needed to assess the generalizability of the results to other populations and countries and to identify characteristics of participants who are most likely to benefit from acupuncture.

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References

1. **Nickel JC, Nyberg LM, Hennenfent M.** Research guidelines for chronic prostatitis: consensus report from the first National Institutes of Health International Prostatitis Collaborative Network. Urology. 1999; 54:229-33. [PMID: 10443716]
2. **Krieger JN, Riley DE, Cheah PY, et al.** Epidemiology of prostatitis: new evidence for a world-wide problem. World J Urol. 2003; 21:70-4. [PMID: 12712363]
3. **Jackson T, Thomas S, Stabile V, et al.** Prevalence of chronic pain in low-income and middle-income countries: a systematic review and meta-analysis. Lancet. 2015;385 Suppl 2:S10. [PMID: 26313056] doi:10.1016/S0140-6736(15)60805-4
4. **Wenninger K, Heiman JR, Rothman I, et al.** Sickness impact of chronic nonbacterial prostatitis and its correlates. J Urol. 1996;155:965-8. [PMID: 8583619]
5. **McNaughton Collins M, Pontari MA, O'Leary MP, et al; Chronic Prostatitis Collaborative Research Network.** Quality of life is impaired in men with chronic prostatitis: the Chronic Prostatitis Collaborative Research Network. J Gen Intern Med. 2001;16:656-62. [PMID: 11679032]
6. **Rees J, Abrahams M, Doble A, et al; Prostatitis Expert Reference Group (PERG).** Diagnosis and treatment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome: a consensus guideline. BJU Int. 2015;116:509-25. [PMID: 25711488] doi:10.1111/bju.13101
7. **Engeler D, Baranowski AP, Berghmans B, et al.** EAU Guidelines on Chronic Pelvic Pain. European Association of Urology; 2021. Accessed at https://uroweb.org/guideline/chronic-pelvic-pain on 29 May 2021.
8. **Alexander RB, Propert KJ, Schaeffer AJ, et al; Chronic Prostatitis Collaborative Research Network.** Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial. Ann Intern Med. 2004;141:581-9. [PMID: 15492337]
9. **Nickel JC, Krieger JN, McNaughton-Collins M, et al; Chronic Prostatitis Collaborative Research Network.** Alfuzosin and symptoms of chronic prostatitis-chronic pelvic pain syndrome. N Engl J Med. 2008;359:2663-73. [PMID: 19092152] doi:10.1056/NEJMoa0803240
10. **Nickel JC, Downey J, Clark J, et al.** Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo-controlled multicenter trial. Urology. 2003;62:614-7. [PMID: 14550427]
11. **Franco JV, Turk T, Jung JH, et al.** Pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. Cochrane Database Syst Rev. 2019;10:CD012552. [PMID: 31587256] doi:10.1002/14651858.CD012552.pub2
12. **Chen Y, Wu X, Liu J, et al.** Effects of a 6-month course of tamsulosin for chronic prostatitis/chronic pelvic pain syndrome: a multicenter, randomized trial. World J Urol. 2011;29:381-5. [PMID: 20336302] doi:10.1007/s00345-010-0537-3
13. **Mehik A, Alas P, Nickel JC, et al.** Alfuzosin treatment for chronic prostatitis/chronic pelvic pain syndrome: a prospective, randomized, double-blind, placebo-controlled, pilot study. Urology. 2003;62:425-9. [PMID: 12946740]
14. **MacPherson H, Vertosick EA, Foster NE, et al; Acupuncture Trialists' Collaboration.** The persistence of the effects of acupuncture after a course of treatment: a meta-analysis of patients with chronic

pain. Pain. 2017;158:784-93. [PMID: 27764035] doi:10.1097/j.pain.0000000000000747
15. **Wang H, Yang G, Wang S, et al.** The most commonly treated acupuncture indications in the United States: a cross-sectional study. Am J Chin Med. 2018:1-33. [PMID: 30298749] doi:10.1142/S0192415X18500738
16. **Franco JV, Turk T, Jung JH, et al.** Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. Cochrane Database Syst Rev. 2018;5:CD012551. [PMID: 29757454] doi:10.1002/14651858.CD012551.pub3
17. **Chang SC, Hsu CH, Hsu CK, et al.** The efficacy of acupuncture in managing patients with chronic prostatitis/chronic pelvic pain syndrome: a systemic review and meta-analysis. Neurourol Urodyn. 2017;36:474-81. [PMID: 26741647] doi:10.1002/nau.22958
18. **Qin Z, Zang Z, Zhou K, et al.** Acupuncture for chronic prostatitis/chronic pelvic pain syndrome: a randomized, sham acupuncture controlled trial. J Urol. 2018;200:815-22. [PMID: 29733836] doi:10.1016/j.juro.2018.05.001
19. **Qin Z, Liu Y, Zhou K, et al.** Acupuncture for chronic prostatitis/chronic pelvic pain syndrome: study protocol for a randomized controlled trial. Trials. 2017;18:616. [PMID: 29273095] doi:10.1186/s13063-017-2383-8
20. **Nickel JC, Shoskes D, Wang Y, et al.** How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome. J Urol. 2006;176:119-24. [PMID: 16753385]
21. **Krieger JN, Nyberg L Jr, Nickel JC.** NIH consensus definition and classification of prostatitis [Letter]. JAMA. 1999;282:236-7. [PMID: 10422990]
22. **Zhou K, Fang J, Wang X, et al.** Characterization of de qi with electroacupuncture at acupoints with different properties. J Altern Complement Med. 2011;17:1007-13. [PMID: 21999154] doi:10.1089/acm.2010.0652
23. **Litwin MS, McNaughton-Collins M, Fowler FJ Jr, et al.** The National Institutes of Health Chronic Prostatitis Symptom Index: development and validation of a new outcome measure. Chronic Prostatitis Collaborative Research Network. J Urol. 1999;162:369-75. [PMID: 10411041]
24. **Propert KJ, Litwin MS, Wang Y, et al; Chronic Prostatitis Collaborative Research Network (CPCRN).** Responsiveness of the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI). Qual Life Res. 2006;15:299-305. [PMID: 16468084]
25. **Rosen RC, Cappelleri JC, Smith MD, et al.** Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999;11:319-26. [PMID: 10637462]
26. **Spaliviero M, Strom KH, Gu X, et al.** Does Greenlight HPS laser photoselective vaporization prostatectomy affect sexual function. J Endourol. 2010;24:2051-7. [PMID: 20964486] doi:10.1089/end.2010.0296
27. **Barry MJ, Fowler FJ Jr, O'Leary MP, et al.** The American Urological Association symptom index for benign prostatic hyperplasia. The measurement committee of the American Urological Association. J Urol. 1992;148:1549-57. [PMID: 1279218]
28. **Zigmond AS, Snaith RP.** The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67:361-70. [PMID: 6880820]
29. **Luo N, Liu G, Li M, et al.** Estimating an EQ-5D-5L value set for China. Value Health. 2017;20:662-9. [PMID: 28408009] doi:10.1016/j.jval.2016.11.016
30. **Herdman M, Gudex C, Lloyd A, et al.** Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). Qual Life Res. 2011;20:1727-36. [PMID: 21479777] doi:10.1007/s11136-011-9903-x
31. **Bang H, Ni L, Davis CE.** Assessment of blinding in clinical trials. Control Clin Trials. 2004;25:143-56. [PMID: 15020033]
32. **Chen J.** BLINDING: Stata module to compute blinding indexes. 2008.
33. **Lee SH, Lee BC.** Electroacupuncture relieves pain in men with chronic prostatitis/chronic pelvic pain syndrome: three-arm randomized trial. Urology. 2009;73:1036-41. [PMID: 19394499] doi:10.1016/j.urology.2008.10.047
34. **Sahin S, Bicer M, Eren GA, et al.** Acupuncture relieves symptoms in chronic prostatitis/chronic pelvic pain syndrome: a randomized, sham-controlled trial. Prostate Cancer Prostatic Dis. 2015;18:249-54. [PMID: 25939517] doi:10.1038/pcan.2015.13
35. **Lee SW, Liong ML, Yuen KH, et al.** Acupuncture versus sham acupuncture for chronic prostatitis/chronic pelvic pain. Am J Med. 2008;121:79.e1-7. [PMID: 18187077] doi:10.1016/j.amjmed.2007.07.033
36. **Nickel JC.** Chronic prostatitis/chronic pelvic pain syndrome: it is time to change our management and research strategy [Editorial]. BJU Int. 2020;125:479-80. [PMID: 32250053] doi:10.1111/bju.15036
37. **Haake M, Müller HH, Schade-Brittinger C, et al.** German Acupuncture Trials (GERAC) for chronic low back pain: randomized, multicenter, blinded, parallel-group trial with 3 groups. Arch Intern Med. 2007;167:1892-8. [PMID: 17893311]
38. **Cherkin DC, Sherman KJ, Avins AL, et al.** A randomized trial comparing acupuncture, simulated acupuncture, and usual care for chronic low back pain. Arch Intern Med. 2009;169:858-66. [PMID: 19433697] doi:10.1001/archinternmed.2009.65
39. **Finniss DG, Kaptchuk TJ, Miller F, et al.** Biological, clinical, and ethical advances of placebo effects. Lancet. 2010;375:686-95. [PMID: 20171404] doi:10.1016/S0140-6736(09)61706-2
40. **Paterson C, Dieppe P.** Characteristic and incidental (placebo) effects in complex interventions such as acupuncture. BMJ. 2005;330:1202-5. [PMID: 15905259]
41. **Lee SW, Liong ML, Yuen KH, et al.** Validation of a sham acupuncture procedure in a randomised, controlled clinical trial of chronic pelvic pain treatment. Acupunct Med. 2011;29:40-6. [PMID: 21245238] doi:10.1136/aim.2010.003137
42. **Lund I, Lundeberg T.** Are minimal, superficial or sham acupuncture procedures acceptable as inert placebo controls. Acupunct Med. 2006;24:13-5. [PMID: 16618044]
43. **Birch S.** A review and analysis of placebo treatments, placebo effects, and placebo controls in trials of medical procedures when sham is not inert. J Altern Complement Med. 2006;12:303-10. [PMID: 16646730]
44. **Han JS.** Acupuncture analgesia: areas of consensus and controversy. Pain. 2011;152:S41-S48. [PMID: 21078546] doi:10.1016/j.pain.2010.10.012
45. **Lee JH, Jang KJ, Lee YT, et al.** Electroacupuncture inhibits inflammatory edema and hyperalgesia through regulation of cyclooxygenase synthesis in both peripheral and central nociceptive sites. Am J Chin Med. 2006;34:981-8. [PMID: 17163587]
46. **Shahed AR, Shoskes DA.** Correlation of beta-endorphin and prostaglandin E2 levels in prostatic fluid of patients with chronic prostatitis with diagnosis and treatment response. J Urol. 2001;166:1738-41. [PMID: 11586213]
47. **Zhang J, Liang C, Shang X, et al.** Chronic prostatitis/chronic pelvic pain syndrome: a disease or symptom? Current perspectives on diagnosis, treatment, and prognosis. Am J Mens Health. 2020;14:1557988320903200. [PMID: 32005088] doi:10.1177/1557988320903200

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