



# Low-intensity extracorporeal shock wave therapy for III B chronic pelvic pain syndrome

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*Contributions:* (I) Conception and design: All authors; (II) Administrative support: L Man; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: G Li; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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**Background:** To analyze the efficiency of low-intensity shock wave therapy (LI-ESWT) for patients with III B chronic pelvic pain syndrome (CPPS).

**Methods:** The study included an uncontrolled population of 32 patients who had suffered with CPPS for  $\geq 3$  months. LI-ESWT was performed without anesthesia via a perineal approach. The operation was carried out in four weeks by administering 12,000 shock waves. Using the Visual Analog Scale (VAS) and NIH-developed Chronic Prostatitis Symptom Index (NIH-CPSI), subsequent tests were performed at 1, 2, 4, and 12 weeks after the first LI-ESWT session.

**Results:** All patients who received the four week course as treatment responded actively on the pain VAS and the NIH-CPSI, and both were significantly improved ( $P < 0.05$ ). Compared with the baseline parameters, the NIH-CPSI total score and VAS exhibited substantial improvement at 4 and 12 weeks, where a total improvement at four weeks was reached. It is easy and safe to perform LI-ESWT without anesthesia on an outpatient basis.

**Conclusions:** LI-ESWT should be regarded as a promising new therapy for CPPS, as it is convenient to perform without any side-effects.

**Keywords:** Chronic pelvic pain syndrome (CPPS); chronic abacterial prostatitis; shock waves

Submitted Sep 27, 2019. Accepted for publication Mar 27, 2020.

doi: 10.21037/tau.2020.04.07

View this article at: <http://dx.doi.org/10.21037/tau.2020.04.07>

## Introduction

Chronic pelvic pain syndrome (CPPS) is considered a regular urological disorder (1). The incidence is stated to be about 15% (2). There are several symptoms of CPPS, such as erectile dysfunction (ED) and pain in the prostate, perineal, and suprapubic regions, which may last for more than three months (3). The patients usually suffer from a lot of pain and restrictions, which are like those after a heart attack, angina pectoris, and Crohn's disease (4).

There are currently no causal or standardized therapeutic approaches to CPPS. Anti-inflammatory agents, analgesics, antibiotics,  $\alpha$ -receptor blockers, and  $5\alpha$ -reductase inhibitors are reported to be used separately or in combination (5,6), but there is no convincing evidence to demonstrate the

efficacy of each treatment type. Consequently, non-drug treatment options have received increased attention. Low-intensity extracorporeal shock wave therapy [low-intensity extracorporeal shock wave therapy (LI-ESWT)] has so far been used to treat musculoskeletal disorders (7), male ED (8), non-healing wounds (9), and myocardial infarction (10). This study will focus on evaluating the effectiveness and safety of LI-ESWT on patients with CPPS.

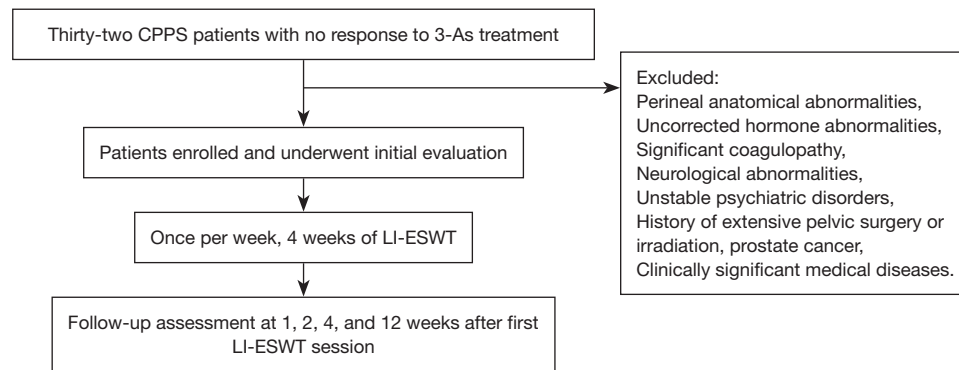
## Methods

### *Inclusion and exclusion criteria*

Patients with CPPS refractory to the traditional 3-As therapy (antibiotics, alpha-blockers, and anti-

**Table 1** The inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Patients who had type IIIB prostatitis/CPPS for more than 3 months, took a combination of at least one course lipophilic antibiotic, simple analgesia and alpha blocker, and other traditional modalities of CPPS treatment did not affect them	Patients with perineal anatomical abnormalities, uncorrected hormone abnormalities, significant coagulopathy, neurological abnormalities, unstable psychiatric disorders, history of extensive pelvic surgery or irradiation, prostate cancer, and clinically significant medical diseases
CPPS, chronic pelvic pain syndrome.	

**Figure 1** Low-intensity extracorporeal shock wave therapy for chronic pelvic pain syndrome: flow chart. CPPS, chronic pelvic pain syndrome; LI-ESWT, low-intensity extracorporeal shock wave therapy.

inflammatories) were enrolled from Beijing Jishuitan Hospital between May 2018 and July 2019. Participants gave informed consent before the study. The local ethics committee approved the study. The study inclusion and exclusion criteria are seen in *Table 1*.

### Treatment protocol

The patients received LI-ESWT treatment once a week for four weeks in an outpatient setting without local or systemic anesthesia. At each therapy session, 3,000 impulses were applied on the perineum at 6 different anatomical sites, with a total energy flow density of 0.25 mJ/mm<sup>2</sup>, 3 Hz. After every 500 pulses, the location of the shock wave transducer was changed to virtually scan the entire area of the prostate and pelvic floor. In the supine position, LI-ESWT was performed. The duration of treatment for each participant was 18 min. An electro-pneumatic shock wave unit with a shock wave source (MASTERPULS, MP100, Storz Medical, Tägerwilen, Switzerland) was used for this study.

### Evaluation of outcomes

The grade of pain was measured using a Visual Analog Scale

(VAS, 0–10). Validated questionnaires [specific complaints with the NIH chronic Prostatitis Symptom Index (CPSI)] were used to investigate the CPPS-related complaints. The follow-up assessments were carried out at 1, 2, 4, and 12 weeks after the first LI-ESWT session. Any adverse effects associated with LI-ESWT were recorded during the follow-up (*Figure 1*).

### Statistical analysis

Methods of descriptive analysis were used to check the data sets. Quantitative data were expressed as means ± standard deviations (SD). Mann-Whitney U test was used to analyze the statistical differences. P<0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

### Results

Thirty-two patients were included, with a mean age of 36±13 years. The mean CPPS history was 33 months (range, 6–36 months). After four weeks of a course of treatment, all of the patients took the pain VAS and the NIH-CPSI, and both were significantly reduced (P<0.05; *Table 2*).

**Table 2** Change of clinical symptoms after LI-ESWT

Sample, weeks	Timepoint				
	Baseline	Week 1	Week 2	Week 4	Week 12
Pain score (items 1–4)	12.43±5.40	10.71±4.86	9.86 ±4.05	5.43±3.67 <sup>a</sup>	7.43±4.18 <sup>a</sup>
Urinary score (items 5–6)	4.57±3.76	4.14±3.3	3.71±3.27	2.86±2.51	3.43±3.13
QoL (items 7–9)	9.14±2.38	9±3.09	8.71±3.27	7.86±3.57	8.71±3.17
NIH-CPSI (items 1–9)	26.14±9.26	23.86±8.51	22.29±7.46	16.14±6.09 <sup>a</sup>	19.57±7.31 <sup>a</sup>
VAS	6.14±2.86	5.29±2.92	4.86±2.25	3±1.84 <sup>a</sup>	4±1.66 <sup>a</sup>

<sup>a</sup>, statistically significant difference compared with the first values between corresponding groups. VAS, Visual Analog Scale; QoL, quality of life; NIH-CPSI, National Institutes of Health Chronic Prostatitis Symptom Index; LI-ESWT, low-intensity extracorporeal shock wave therapy.

For each domain, the NIH-CPSI has been evaluated as shown above. The score of pain domain, as well as the total score, showed significant improvement at week 4, and the treatment effect could be preserved until week 12 ( $P<0.05$ ).

Compared with baseline parameters such as NIH-CPSI total score and VAS, the NIH-CPSI total score and VAS showed significant improvement at weeks 4 and 12, and the highest change was reached at week 4. Meanwhile, the other parameters showed the maximum effect at 4 weeks but a slight deterioration at week 12. No significant side effects were observed, and it is unnecessary for any type of analgesia during the whole course of treatment.

## Discussion

There are only hypothetical models for the pathogenesis of CPPS so far. The pathophysiology of CPPS has not yet been explained. The manifestations of CPPS often comprise a myofascial pain syndrome, an abnormal tone of the periprostatic musculature, an increasingly visible neurological component, and dysfunctional effects (11,12). There were many complaints associated with the autonomous nervous system and the interplay between smooth and cross-striated muscles. Acute and chronic inflammations involved sympathetic endplate, which may result in the endogenous generation of pain via nociceptive nerve endings and receptors. Furthermore, some psychological stress may result in abnormal electromyographic activity and myofascial pain syndromes (13). Therefore, it is feasible to use myofascial trigger points, cognitive behavioral therapy, and biofeedback and relaxation training to treat those disorders associated with CPPS (14).

Low-intensity extracorporeal shock waves, as a kind of electro-pneumatic shock wave, were transformed into biochemical signals in a process named mechanotransduction,

which may hyperstimulate nociceptors and interrupt the former pain memory nerve impulses to achieve ‘reprogramming’ (15). Furthermore, cavitation bubbles will be generated and popped, which may regenerate secondary energy waves called microjets that lead to additional mechanical forces, increase local microvasculature (16), reduce pain, and help to heal tissue (17).

LI-ESWT has effects on the periprostatic pelvic floor muscles. Consequently, local muscle relaxation may result in the disorder improving due to a reduction in functional muscle shortening (18). This mechanism showed the short-term effect of the shock waves, since the pain sensation may be prevented relatively transiently without enduring modulation in the sensitivity of the treatment area. In the present study, according to the follow-up of 12 weeks, the VAS and NIH-CPPS were significantly improved, the pain intensity associated with CPPS was reduced by about half, the maximum alleviation was at 4 weeks after the first treatment session, and the pain slightly increased at 12 weeks after LI-ESWT. However, the therapeutic effect was still significant. As expected, the patients’ symptoms were improved via pain reduction by LI-ESWT, which was still valid over several weeks. In our research, the length of follow-up was limited to 12 weeks (16,19–22). The longer-term effect of LI-ESWT may involve some other mechanisms. In previous studies, LI-ESWT induced cell membrane modifications and functional changes and conducted a series of cell signaling and biological activation processes, such as cell proliferation, angiogenesis, peripheral nerve regeneration, increased cell permeability, and anti-inflammation (23,24).

It is noted that limited studies on LI-ESWT have reported the improvement of CPPS (16,19–22,25–27). In the current investigation, studies reported since 2008 were reviewed and are listed in *Table 3*. Zimmermann *et al.* first

Table 3 Literature review of studies about LI-ESWT in patients with chronic pelvic pain syndrome

Author	Study design	Generator	Patient number	Follow-up (weeks after ESWT)	Energy density (mJ/mm <sup>2</sup> )	No. of pulses each treatment	No. of treatments each week	Treatment courses (weeks)	NIH-CPSI [week]	CPSI↓ ≥6 [week]	VAS [week]	IPSS [week]
Zimmermann <i>et al.</i> , 2008 (19)	CS	Minilith SLI	14	1, 4, 12	0.11	2,000	3	2	-2.7 [12]	-	-31 [12]	NA
Zimmermann <i>et al.</i> , 2008 (19)	CS	Duolith SDI	20	1, 4, 12	0.25	3,000	1	4	-8.6 [1]	-	-2.4 [1]	-4.1 [1]
Zimmermann <i>et al.</i> , 2009 (16)	RCT	Duolith SDI	30	1, 4, 12	0.25	3,000	1	4	-16.7 [1]	-	-33.3 [1]	-15.6 [1]
Zeng <i>et al.</i> , 2012 (20)	RCT	HB-ESWT-01	8	4, 12	0.06-maximum tolerated dose	2,000	5	2	-	21.1% [4]	NA	NA
Vahdatpour <i>et al.</i> , 2013 (21)	RCT	Duolith SDI	40	1, 2, 3, 12 after first LI-ESWT session	0.25-0.4 (0.05 mJ/mm <sup>2</sup> was added in each week)	3,000	1	4	-5.1 [1]	-	-2.0 [1]	-1.0 [1]
Moayednia <i>et al.</i> , 2014 (25)	RCT	Duolith SDI	19	16, 20, 24	0.25	3,000	1	4	-10.2 [3]	-	-5.1 [3]	-1.73 [3]
Pajovic <i>et al.</i> , 2016 (26)	RCT	KM-2000S	30	12, 24	0.25	3,000	1	4	-7.1 [12]	-	-4.3 [12]	-0.9 [12]
Al Edwan <i>et al.</i> , 2017 (27)	CS	E-S.W.T Roland	41	2, 24, 48	0.25	2,500	1	4	-4.47 [16]	-	-2.66 [16]	-0.71 [16]
Guu <i>et al.</i> , 2018 (22)	CS	Duolith SDI	33	1, 4, 12	0.25	3,000	1	4	-1.06 [20]	-	-1.24 [20]	-0.39 [20]
									+0.38 [24]	-	+0.53 [24]	+0.12 [24]
									-17.4 [24]	-	-9.2 [24]	-3.2 [24]
									-9.2 [2]	-	-4.1 [2]	-5.9 [2]
									-8.8 [24]	-	-3.5 [24]	-6.6 [24]
									-8.2 [48]	-	-3.2 [48]	-6.6 [48]
									-9.06 [4]	75.8% [4]	-2.38 [4]	-5.18 [4]
									-12.97 [12]	81.8% [12]	-3.29 [12]	-5.97 [12]

IPSS, International Prostate Symptom Score; LI-ESWT, low-intensity extracorporeal shock wave therapy; NA, not available; NIH-CPSI, National Institutes of Health-Chronic Prostatitis Symptom Index; RCT, randomized controlled trial; CS, cohort study; VAS, Visual Analog Scale.

reported using LI-ESWT for the treatment of CPPS in 2008 (19). Five included trials were randomized controlled trials with sham therapy (16,20,21,25,26). However, most of the included trials had small samples. The largest sample included in these reviews was only 41 patients (27). In most of the studies, follow-up was restricted to 12 weeks, while in some studies it was as long as 24 weeks. The long-term effect of LI-ESWT is still equivocal (25-27). According to the literature review in *Table 3*, both of the cohort and randomized controlled studies revealed statistically significant improvements in NIH-CPSI, QOL, and the pain domain scores after LI-ESWT in short-term follow-up (16,19-22,25-27).

The weakness of our study was that it employed an open-label clinical trial lacking a controlled group and a small sample size. In our study, the number of shock waves and the energy level were decided empirically. Furthermore, as discussed above, the term of follow-up was only 12 weeks. The number of treatments, the treatment intervals, and the number of pulses per session was calculated from previous clinical application trials, so it is uncertain which formulation should be used in the treatment protocol. The present mechanisms cannot explain the longer-term effect of LI-ESWT. Compared with week 1, there was some deterioration in total NIH-CPSI, pain, the urinary scores, and QoL at week 24 of follow-up in some studies (25-27).

The strength of our study was that all of our included patients did not achieve satisfactory results from all other traditional modalities of treatments such as combined alpha-blockers, simple analgesia, and antibiotics. There were no significant side-effects during or after treatment, and it is convenient for the patients to undergo an out-patient treatment. However, it is still necessary to define a sufficient therapeutic protocol such as energy density, probe location, pulse numbers, and session numbers, and to determine crucial predict factors regarding successful response to LI-ESWT in patients with CPPS.

In conclusion, LI-ESWT may be considered necessary for CPPS treatment, since it is convenient to apply without side effects. For the first time, it is possible to employ LI-ESWT to provide a rapid and thrifty outpatient therapeutic option for CPPS by using a standard unit as well as a treatment which was time-saving and can be repeated as demanded. A double-blind placebo-controlled study, including a sham treatment and an extended follow-up, is expected for further evaluation of this method.

## Acknowledgments

*Funding:* This work was supported by the Beijing Municipal Science & Technology Commission No. Z171100001017133.

## Footnote

*Conflicts of Interest:* Both authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tau.2020.04.07>). Both authors report grants from Beijing Municipal Science & Technology Commission, during the conduct of the study.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The local ethics committee approved the study (No. 201901-07). Participants gave informed consent before the study.

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**Cite this article as:** Li G, Man L. Low-intensity extracorporeal shock wave therapy for III B chronic pelvic pain syndrome. *Transl Androl Urol* 2020;9(3):1323-1328. doi:10.21037/tau.2020.04.07