

# The Effects of Combining Perineal ESWT and Triple Therapy versus Perineal ESWT alone for the Treatment of Non-Inflammatory CPPS (Category III B)

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**Abstract:** ***Objective:** To compare the additional effect of combination therapy of extracorporeal shockwave therapy (ESWT) and medical treatment on chronic prostatitis type IIIB chronic pelvic pain syndrome (CPPS) with the effect of perineal ESWT alone. **Material and methods:** A prospective single-blind comparative study that included 40 Cases collected from February 2022 to October 2022. Patients were divided into two groups each is 20 patients. The first group received a combination of ESWT, and the triple therapy of an alpha-blocker called group C, an anti-inflammatory agent, and a muscle relaxant. The second group treated with an ESWT alone was called group E. **Results:** Both groups showed improvement in all the National Institute of Health Chronic Prostatitis Symptom Index (NIH-CPSI) domains with more than a six-point decline in the NIH-CPSI total score in both groups. There are significantly superior results in the patients who were in group C and this improvement was statistically significant only after 6 months from starting treatment in the pain domain, urinary domain, and in the total score, p-values 0.002, 0.002, 0.001 respectively. **Conclusion:** Patients who were on a combination of ESWT and triple medication and patients who were on ESWT showed significant improvement in all items of the NIH-CPSI score during the treatment, with significantly superior results in the Patients who were on a combination of ESWT and triple medication.*

**Keywords:** Pain, Extracorporeal Shock Wave Therapy, Prostatitis

## 1. Introduction

Chronic pelvic pain syndrome (CPPS) refers to the presence of chronic pelvic pain (CPP) with no identified pathology, in comparison to 'specific disease-associated pelvic pain' in which an underlying pathology is identified (such as cancer or infection) [1, 2]. It is often associated with negative cognitive, behavioral, sexual, or emotional consequences, as well as with symptoms suggestive of the lower urinary tract, and sexual, bowel, or gynecological dysfunction [3]. CPPS is one of the most common diseases in urology, with a prevalence in population-based surveys in the range of 3–10% and affects around 15% of all urologic outpatients. In the general population chronic pelvic pain syndrome occurs in about 0.5% in a given year [4].

The cause of CPPS is unknown and there are no well-conducted epidemiological studies to support any particular risk factor [5, 6]. The failure to find a single etiological agent has hampered the identification of curative interventions for CP/CPPS. It has been hypothesized that infection (occult or non-culturable infection included), as well as genetic, anatomical, physiological, neurological, and immunological factors, may be involved (alone or combined) in the pathogenesis of CP/CPPS. In this regard,

that different cases of CP/CPPS are likely to have different etiological determinants and different disease progression pathways [7].

Directed 3-A therapy (antibiotics, alpha-blockers, and anti-inflammatories), rather than monotherapy, is often used as a first-line treatment for patients with CPPS because of its convenience and good efficacy) [8]. Low-intensity extracorporeal shock wave therapy (LI-ESWT), a noninvasive therapy, has been applied recently in the treatment of CPPS because it can induce neovascularization and anti-inflammation, nerve impulse interruption, reduce passive muscle tone, influence neuroplasticity of the pain memory, extracorporeal shock waves at a low-energy-density could enhance improvement of pain, urination, erectile function, and QoL. Although most of the published results identified that LI-ESWT can be a useful treatment for patients with CPPS [9]. The current study aimed to compare the additional effect of combination therapy of ESWT and medical treatment on chronic prostatitis type IIIB CPPS with the effect of transperineal ESWT alone.

## 2. Method

### 2.1 Study design and setting

A prospective single-blinded comparative study in which 40 Cases collected at Gazi Al Hariri hospital from February 2022 to October 2022 their ages 22-54 years were diagnosed with chronic prostatitis type IIIB.

### 2.2 Data collection

The diagnosis of Category III B CPPS included a detailed history, physical examination and digital rectal examination, PSA measurement, standard microbiologic cultures, and microscopic analysis of urine (before and after prostatic massage).

Patients were divided randomly into two groups: **The first group (group C)** included 20 patients who accepted the treatment with a combination of ESWT therapy and the triple therapy of an  $\alpha$ -blocker, an anti-inflammatory agent, and a muscle relaxant. **The second group (group E)** included 20 patients, who were treated with an ESWT alone.

Patients were assessed by the NIH Chronic Prostatitis Symptom Index (NIH-CPSI) at the initiation of therapy, as well as at 2 weeks, 3 months, and 6 months from initiation of therapy.

### 2.3 Inclusion criteria

Chronic prostatitis type IIIB/chronic pelvic pain syndrome, six months duration of symptom

### 2.4 Exclusion criteria

Those who had significant medical or neurological problems that could affect lower urinary tract function and Patients with a history of urethral instrumentation or transurethral surgery.

### 2.5 History and physical examination

Every patient exhibited symptoms for at least 6 months. Patients were carefully examined by inspection and palpation of the external genitalia and digital rectal examination.

### 2.6 Pre-massage and post-massage urine test (PPMT)

Segmented urine collection was used and the PPMT was made according to the "2-glass test" method [8].

### 2.7 Medications and ESWT therapy

**Group C** received a combination of ESWT and triple therapy which consisted of a combination of an  $\alpha$ -blocker (Tamsulosin) 0.4mg/day an anti-inflammatory (diclofenac sodium SR)100 mg/day and a muscle relaxant (baclofen) 5mg/3 times a-day then after 3 days 10 mg 3 times daily and the combination used for 3 months. **Group E** patients were treated with ESWT alone.

Patients during ESWT receiving one focused perennally applied ESWT treatment weekly, for 6 weeks; in each session 3000 Impulses were applied and the position of the probe changed every 500 impulses with a total energy flow density of 0.25 mJ/mm<sup>2</sup>, frequency 3 Hz and the duration of ESWT was 14 min each. The device used an Electromagnetic SW device with a focused SW source (Duolith SD1, Storz Medical). Patients were evaluated after 2 weeks of the treatment and followed post-treatment, with evaluation after 3 months and 6 months post-treatment.

### 2.8 Ethical approval

Ethical committee approval was received from the Ethics Committee of Iraqi Board for Medical Specialization (Approval No: 2021/0135). Written informed consent taken from all the patients in accordance with Helsinki declaration of human studies.

### 2.9 Sample Size Estimation

Convenient sample that involved 80 patients recruited in the study.

### 2.10 Statistical analysis

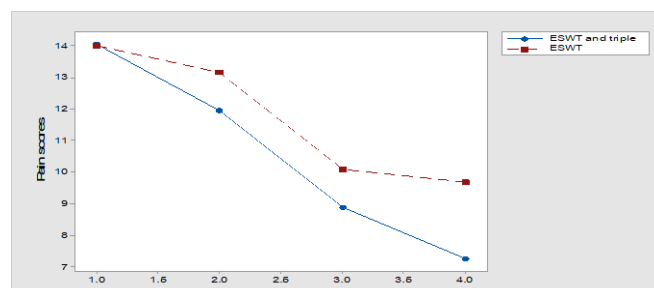
Following the customary methods of statistical description, the Student T test was applied. The difference in the obtained values was considered to be significant when the p value was less than 0.05.

## 3. Results

The age of the patients in this study ranged from ((22 – 54)) years. The mean ages in group C were  $38.6 \pm 8.8$  years, and the mean ages in group E were  $30.3 \pm 8.5$  years. In this study, there was no difference in the ages in both groups p-value of 0.302.

### 3.1 Regarding the Pain domain

The scores in both groups were reduced during the first 2 weeks and 3 months but this reduction was not statistically significant at 2 weeks and 3 months, Then the difference became statistically significant after 6 months. The rate of mean change in pain scores regarding group C was 48.25% and group E was 30.7%, as illustrated by table 1 and figure 1.



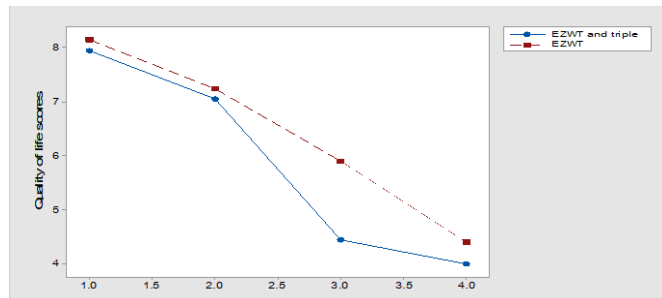
**Figure 1:** Comparison of change in pain scores, between the 2 groups. (1.0: baseline, 2.0: 2weeks, 3.0: 3months, and 4.0: 6months)

### 3.2 Regarding the Urinary symptoms scores domain

There was a decrease in urinary scores in group E mainly after 6 months **p-value of 0.005** and the mean reduction in urinary scores was 75 % in group C and 61% in group E.

### 3.3 Regarding quality-of-life domain

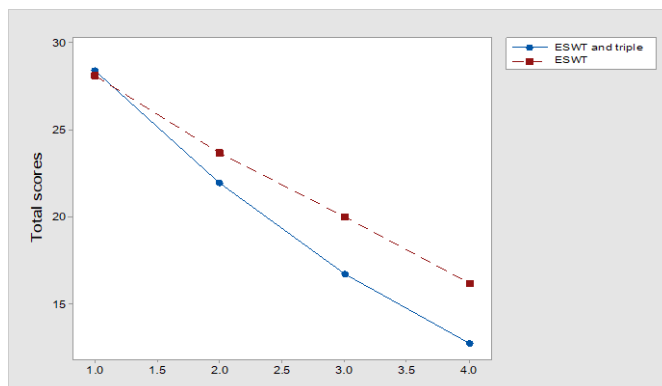
There was a decrease in the quality-of-life score in both study groups, but it was not statistically significant till the end of the study, mean reduction in both groups was 49.6% in group C and 46.01 % in group E, as illustrated in table 1 and in figure 2.



**Figure 2:** Comparison of change in quality-of-life scores, between the 2 groups. (1.0: baseline, 2.0: 2weeks,3.0: 3months, and 4.0: 6months).

### 3.4 Total scores

There was a reduction in total scores in both of the study groups, but it was not statistically significant until the 6 months p-value of 0.001. The mean reduction in total scores in group C was 54.93% and in group E 42.27%.



**Figure 3:** Comparison of total scores between the 2 groups. (1.0: baseline, 2.0: 2weeks,3.0: 3months, and 4.0: 6months).

The patient's group on ESWT didn't complain of any side effects during treatment. while patients on ESWT and triple medication (N:20) had few side effects. Gastrointestinal upset (2 patients), Palpitation (1 patient), Dizziness (1 patient), and Postural hypotension (1 patient). The total percentage of side effects was 25 % in the group of patients on ESWT and triple medication, as illustrated in figure 3 and table 1.

**Table 1:** Comparison between the two groups during the treatment

	Group C	Group E	p-value
<b>Pain score</b>			
Baseline	14.05±3.44	14 ±3.67	0.965
2 weeks	11.95±3.19	13.15±3.35	0.965
3 months	8.9±2.63	10.1±3.27	0.209
6 months	7.27±1.91	9.7±2.83	0.002
<b>Urinary scores</b>			
Baseline	6.4±1.60	6±1.72	0.451
2 weeks	4.2±1.57	6±1.72	0.501
3 months	3±1.49	3.3±1.3	0.08
6 months	1.6±0.75	2.3±0.73	0.005
<b>Quality of life scores</b>			
Baseline	7.95±1.54	8.15±1.98	0.723
2 weeks	7.05±1.57	7.25±1.62	0.694
3 months	5.45±1.32	5.9±1.37	0.297
6 months	4±1.41	4.4±1.47	0.385
<b>Total scores</b>			
Baseline	28.4±3.78	28.15±6.26	0.879
2 weeks	22±3.23	23.7±4.54	0.181
3 months	16.75±3.54	20±4.04	0.01
6 months	12.8±2.78	16.25±3.01	0.001

## 4. Discussion

Both groups showed improvement in all NIH-CPSI domains with more than a six-point decline in the NIH- CPSI total score in both groups. Which represents the optimal threshold for predicting treatment response [10]. There was no statistical difference in the meaning of both groups at the baseline before starting the treatment. The improvement in the pain score may be because ESWT causes Hyperstimulation of nociceptors and interrupting the flow of nerve impulses could lead to pain alleviation [11], with the added effect of NSAIDs and their analgesic effect. The improvement in the urinary score may be the added effect of ESWT which causes The periprostatic pelvic floor muscles relaxation [11], to the effects of medications alpha-blockers and muscle relaxants in the combination therapy. Till now theirs is no study comparing ESWT and triple medication versus ESWT. The average follow-up in most studies was 3 months after ESWT.

Zimmermann et al A randomized double-blind study of ESWT in patients with CPPS showed that all outcome parameters improved significantly in the treatment group at month 3 (NIH-CPSI: 17% decrease), with no improvement in the sham-treated group. This is the first study to recommend level 1 evidence for ESWT in patients with CPPS [11].

Vahdatpour et al showed that Pain domain scores at follow-up points in both treatment and sham groups were reduced, more so in the treatment group, which were significant at weeks 2, 3, and 12. Urinary scores became significantly different at weeks 3 and 12. Also, quality of life and total NIH-CPSI scores [12].

Nikolaevich et al In their study 30 patients were divided into 2 groups the first group, patients were treated by ESWT. The second group received pharmacological treatment. The study revealed perineal ESWT as a safe and effective therapy

option for CPPS with more significant effects in comparison to pharmacological treatment after 3 months [13].

Some studies extended their follow-up ranging from 24 weeks to one year. Moayednia et al. showed that at week 24 of follow-up, the mean scores of pains, urinary symptoms, quality of life, and total NIH-CPSI score were not statistically different from baseline in the ESWT group [14]. While in another study by Al Edwan et al it showed statistically significant improvement in all parameters with the maintenance of the effect without any significant side-effect of the treatment over the 12 months [15].

It seems that further studies are needed to determine its long-term efficacy. Pajovic et al compared two groups: the first group given perennially applied ESWT with triple therapy as a combination versus triple therapy alone and followed for 9 months. They were the superior result in the first group than the triple therapy alone group [16].

Rayegani et al compared two groups: the first group given perennially applied ESWT with triple therapy as a combination versus triple therapy and sham ESWT, the difference became significant at weeks 4 and 12 after treatment for NIH-CPSI total and subdomain scores in favor of ESWT group [17]. And both studies showed the superiority of the combination therapy of ESWT and triple medication in the treatment of CPPS as in our study. But in our study, the quality-of-life domain improved in both groups during all phases of follow-up, but it wasn't statistically significant unlike other parameters could this be attributed to the systematic side effect and the duration of triple medication 3 months.

## 5. Conclusions

Patients who were on a combination of ESWT and triple medication and patients who were on ESWT showed significant improvement in all items of the NIH-CPSI score after the treatment, with significantly superior results in the Patients who were on a combination of ESWT, and triple medication and it was statistically significant only after 6 months in all domains of NIH-CPSI except the quality-of-life domain. The drawback to the combination of ESWT and triple medication is the systemic side effect of the medical treatment. ESWT is a safe procedure and free of complications and can be done as an outpatient procedure. ESWT may in particular be interesting because of its easy and inexpensive application, and the potential for repetition of the treatment at any time.

## 6. Recommendations

A larger sample size with a more extended follow period to know the long-term effect of the combination of ESWT and triple medication. using a more detailed investigation like Uroflowmetry and post-void residual volume for follow-up patients with CPPS III B.

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