Extracorporeal shock wave therapy in the treatment of chronic calculous prostatitis


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Extracorporeal shock wave therapy (ESWT) is known as an effective method for inflammatory diseases treatment of various localization. It is actual and perspective treatment methods for chronic calculous prostatitis (CCP).

The objective: to evaluate the dynamics and interrelationships of clinical symptoms, twinkling artifact, the levels of leukocytes and cytokines in the ejaculate during the use of ESWT for the treatment of patients with CCP.

Materials and methods. The study included 37 patients with aged 18–45 years with CCP after ESWT in the projection of the prostate gland (PG). The participants of the study were assessed for prostatitis symptoms according to the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), depression symptoms - Patient Health Questionnaire-9 (PHQ-9); anxiety symptoms – Generalized Anxiety Disorder-7 (GAD-7), sexual dysfunction symptoms – International Index of Erectile Function (IIEF).

Patients had ultrasonographic examination of the pelvic organs with the determination of a twinkling artifact. The levels of IL-1β and IL-10 in ejaculate before and after treatment were determined using enzyme immunoassay. For the analysis of the treatment results, the patients with a significant reduction in the activity of symptoms of PG (by 6 or more points on the NIH-CPSI scale) were included in subgroup A. The patients with insufficient efficacy were involved in subgroup B.

Results. A clinically significant reduction in the severity of prostatitis symptoms (by 6 or more NIH-CPSI points) as a result of treatment was observed in 27 (72.9%) patients. The total prostatitis symptom score (NIH-CPSI) (p<0.05), as well as domains of pain, dysuria and impact on patients’ quality of life, intensity of symptoms of depression, anxiety and erectile dysfunction changed significantly. Changes in the IL-1β and IL-10 concentrations in the ejaculate did not depend on the clinical improvement of the patients’ condition.

Before treatment, the concentration of IL-1β in the ejaculate was positive correlated with the index of depression symptoms (r=0.381, p=0.020) and negative correlated with the indicators of erection, orgasm and sexual desire (r=-0.326, p=0.049; r=-0.329, p=0.046; r=-0.389, p=0.017, respectively). After treatment, the concentration of IL-1β in the ejaculate was positive correlated with the general assessment of prostatitis symptoms, quality of life and anxiety symptoms (r=0.339, p=0.040; r=0.358, p=0.029; r=0.334, p=0.044, respectively), and also negative correlated with indicators of orgasm and sexual desire (r=-0.421, p=0.009; r=-0.455, p=0.005, respectively).

A decrease in the frequency of twinkling artifact in the PG projection was found. At the same time, no significant changes in the presence of echo-positive inclusions were detected. Before treatment, a significant correlation of the presence of twinkling artifact was determined with the total score of prostatitis symptoms (r=0.448, p=0.005), domains of pain (r=0.404, p=0.013) and quality of life (r=0.331, p=0.045), orgasm (r =-0.469, p=0.003) and sexual desire (r=-0.530, p=0.034). No correlation was found with other investigated indicators.

Conclusions. The results of the study demonstrated that ESWT provides a significant reduction in symptoms of prostatitis, anxiety, depression and erectile dysfunction through a dosed anti-inflammatory and anticalcification effect on the PG. The use of Doppler twinkling artifact can be useful for characterizing and monitoring the treatment of PG calcifications.

Keywords: chronic prostatitis, prostate calcifications, extracorporeal shock wave therapy, ejaculate interleukins, twinkling artifact.
Пациенти виконували ультрасонографічне дослідження органів малого таза з визначенням миготливого артефакту. За допомогою іммуноферментного аналізу визначали рівні IL-1β та IL-10 в еякуляті та після лікування. Для аналізу результатів лікування пацієнти із значним зменшенням симптомів ПЗ (на 6 більше балів за шкалою NIH-CPSI) були включені у підгрупу А. Пацієнти з недостатньою ефективністю були об’єднані в підгрупу Б.

Результати. Клінічно значуще зменшення активності симптомів простатиту (на 6 та більше балів NIH-CPSI) внаслідок лікування спостерігали у 27 (72,9%) пацієнтів. Значуще зменшилась загальний бал оцінки симптомів простатиту (NIH-CPSI) (р<0,05), а також домені боля, дисуриї та впливу на якість життя пацієнтів, інтенсивність симптомів депресії, тривоги та еректильної дисфункції.

Зміни відбулися через 12 та 24 тижні після лікування. Результати досліджень свідчать, що ESWT забезпечує значне зменшення симптомів у 27 (72,9%) пацієнтів. Значущі зміни представлені у табл. 1. На середню частоту виявлення миготливого артефакту у проекції ПЗ значущих змін не виявлено. Зафіксовано зменшення частоти виявлення миготливого артефакту у проекції ПЗ. Водночас значущих змін не виявлено в структурних змінах миготливого артефакту.

Ключові слова: хронічний простатит, кальцинати передміхурової залози, екстракорпоральна ударно-хвильова терапія.
MATERIALS AND METHODS
The study included 37 patients aged 18–45 years with chronic calculous prostatitis without signs of infection (CP/CPPS on the background of prostatic calcification) who underwent ESWT for projection of the prostate gland and seminal vesicles. We evaluated the dynamics of prostatitis symptoms according to the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI), symptoms of depression – Patient Health Questionnaire-9 (PHQ-9); anxiety symptoms – Generalized Anxiety Disorder-7 (GAD-7), symptoms of sexual dysfunction – International Index of Erectile Function (IIEF). Cytokines in the ejaculate were also determined before and after treatment using enzyme-linked immunosorbent assay [28, 29, 30].

The level of opportunistic pathogenic microflora in the ejaculate of patients did not exceed 10^4 CFU/ml. The presence of sexually transmitted infections was ruled out by polymerase chain reaction of the ejaculate.

To detect prostate calcification, all patients underwent a transabdominal ultrasound examination with a convex sensor in B-mode gray scale. We determined the presence of echo-positive inclusions (≥ 3 mm) in the prostate gland, as well as a twinkling artifact in the mode of duplex diagnostics, that is, when combining B-mode gray scale and color Doppler mapping. All patients were examined on the Toshiba Xario Expert ultrasound diagnostic system. We considered the twinkling artifact to be a sign of moderate calcification of the prostate parenchyma, which exceeds the intensity of inclusions without an echo-shadow, but which appears earlier than the echo-shadow in the inclusion. It should be noted that the detection of a twinkling artifact was combined with the detection of echo-positive inclusions, with the exception of one case.

Exclusion criteria were the presence of coagulopathy, pelvic and perineal abnormalities, uncorrected neurological, mental, hormonal disorders, malignant oncological diseases, radiation or pelvic surgery in the anamnesis.

All participants received ESWT 2000 shocks (up to 0.25 mJ/mm², 8 Hz), 10 sessions, 2–3 times a week, on an outpatient basis, without anesthesia, but not allowing pain during the procedure. During the study period, the patients did not receive any other treatment. Treatment success was defined as a reduction of 6 points or more on the NIH-CPSI total score. Patients with a successful treatment result for statistical analysis were grouped into subgroup A. Patients with insufficient efficacy were combined into subgroup B. When evaluated up to 14 points according to the NIH-CPSI questionnaire, prostatitis symptoms were considered mild; 15–29 points – moderate; 30–43 points are difficult.

Statistical analysis. Under the conditions of normal distribution, the data are presented in the form of the mean and standard deviation, in the case of non-normal distribution – in the form of the median and 25 and 75 quartiles. The comparison of average indicators in the first protocol, none of them were excluded. As a result of the treatment, the symptoms of prostatitis underwent significant changes. Before treatment, we observed mild prostatitis symptoms in 13.5% of them, moderate symptoms in 83.8%, and severe symptoms in 1 patient (2.7%). After treatment, the condition of most patients improved: mild symptoms were detected in 86.5% and moderate symptoms in 13.5%. As can be seen, the proportion of patients with moderate symptoms of prostatitis significantly decreased after the use of ESWT.

As a result of the treatment, a clinically significant reduction in the activity of prostatitis symptoms (by 6 or more NIH-CPSI points) was observed in 27 (72.9%) patients. These patients were grouped into subgroup A. At the same time, the total score of NIH-CPSI significantly changed (p<0.05), as well as the domains of pain, dysuria, and impact on patients’ quality of life (Table 1).

As a result of the treatment, the intensity of erectile dysfunction, symptoms of depression and anxiety decreased significantly (Table 2).

In the general group, subgroups A and B, the concentration of cytokines in the ejaculate under the

### Table 1

<table>
<thead>
<tr>
<th>Indexes</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH-CPSI Overall score, points Me±σ</td>
<td>19,5±4,8</td>
<td>10,7±4,1*</td>
</tr>
<tr>
<td>Domain of pain points Me (25;75)</td>
<td>7 (6;9)</td>
<td>3 (0;6) *</td>
</tr>
<tr>
<td>Dysuria domain, points Me (25;75)</td>
<td>3 (2;5;5)</td>
<td>2 (1;3) *</td>
</tr>
<tr>
<td>Quality of life, points Me (25;75)</td>
<td>8 (7;9,5)</td>
<td>5 (5;6) *</td>
</tr>
</tbody>
</table>

Note: NIH-CPSI – National Institutes of Health Chronic Prostatitis Symptom index. * – the difference before and after treatment is statistically significant (p<0.05).

### Table 2

<table>
<thead>
<tr>
<th>Indexes</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIEF erection, points Me (25;75)</td>
<td>6.0 (1,0; 12,0)</td>
<td>9.0 (6,0; 12,5) *</td>
</tr>
<tr>
<td>IIEF orgasm, points Me (25;75)</td>
<td>9,0 (0,0; 10,0)</td>
<td>10.0 (10,0, 10,0) *</td>
</tr>
<tr>
<td>IIEF desire, points Me (25;75)</td>
<td>4,0 (2,0; 5,0)</td>
<td>4,0 (4.0, 6,0) *</td>
</tr>
<tr>
<td>IIEF satisfaction with sexual intercourse, points</td>
<td>7,0 (0,0; 8,0)</td>
<td>8,0 (6,0; 9,0) *</td>
</tr>
<tr>
<td>IIEF overall satisfaction, points</td>
<td>4,0 (2,0; 6,0)</td>
<td>6,0 (4,0; 6,0) *</td>
</tr>
<tr>
<td>PHQ-9, points</td>
<td>6,0 (3; 9)</td>
<td>4,0 (0; 6) *</td>
</tr>
<tr>
<td>GAD-7, points</td>
<td>4,0 (0; 7;5)</td>
<td>3,0 (0; 5) *</td>
</tr>
</tbody>
</table>

Note: IIEF – International Index of Erectile Function; PHQ-9 - Patient Health Questionnaire-9; GAD-7 – Generalized Anxiety Disorder-7. * – the difference before and after treatment is statistically significant (p<0.05).
influence of treatment was subject to significant changes (Table 3). However, there was no significant difference in IL-1β and IL-10 between subgroups A and B. Thus, changes in the content of IL-1β and IL-10 in the ejaculate, as a reflection of the impact of the dosed injury of the prostate gland and seminal vesicles with a shock wave, did not depend on the clinical improvement of the patients' condition at the given duration of observation.

The total prostatitis symptom score (NIH-CPSI), as well as pain, dysuria, and quality of life domains, were significantly inversely correlated with scores of all domains of the IIEF questionnaire and directly correlated with scores of depression and anxiety symptoms (Table 4). At the same time, a significant correlation with an increased number of leukocytes, IL-1β and IL-10 was observed.

Before treatment, the concentration of IL-1β in the ejaculate was directly correlated with the index of depression symptoms (r=0.381, p=0.020) and inversely correlated with the indicators of erection, orgasm, and sexual desire (r=-0.326, p=0.049; r=-0.329, p=0.046; r=-0.389, p=0.017; respectively). There was no significant correlation with indicators of prostatitis symptoms, anxiety, pleasure from sexual intercourse and general satisfaction.

After treatment, the concentration of IL-1β in the ejaculate was directly correlated with the general assessment of prostatitis symptoms, quality of life, and anxiety symptoms (r=0.339, p=0.040; r=0.358, p=0.029; r=0.334, p=0.044; respectively), and also inversely correlated with indicators of orgasm and sexual desire (r=-0.421, p=0.009; r=-0.453, p=0.005; respectively).

There were no significant associations between the concentration of IL-10 in the ejaculate with indicators of sexual function, symptoms of prostatitis, depression and anxiety both before and after treatment. Although after treatment, unlike IL-1β, the concentration of IL-10 was significantly inversely correlated with the content of ejaculate leukocytes (r =-0.358, p=0.029). After treatment, the latter was directly correlated with symptoms of depression. Along with this, before the treatment, no correlation was found between the content of leukocytes in the ejaculate and the symptoms of the disease.

**Table 3**

**Dynamics of cytokine concentration (IL-1β, IL-10) in ejaculate**

<table>
<thead>
<tr>
<th>Indexes</th>
<th>До лікування</th>
<th>Після лікування</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1β, pg/ml</td>
<td>156.5±58.7</td>
<td>102.5±49.5*</td>
</tr>
<tr>
<td>IL-1β (Subgroup A), pg/ml</td>
<td>150.3±60.4</td>
<td>103.9±49.1*</td>
</tr>
<tr>
<td>IL-1β (Subgroup B), pg/ml</td>
<td>173.4±52.9</td>
<td>98.8±53.3*</td>
</tr>
<tr>
<td>IL-10, pg/ml</td>
<td>124.3±41.7</td>
<td>176.7±44.8*</td>
</tr>
<tr>
<td>IL-10 (Subgroup A), pg/ml</td>
<td>122.9±46.2</td>
<td>174.0±43.9*</td>
</tr>
<tr>
<td>IL-10 (Subgroup B), pg/ml</td>
<td>127.9±27.8</td>
<td>184.0±48.6*</td>
</tr>
</tbody>
</table>

Note: IL is interleukin, * – the difference before and after treatment is statistically significant (p<0.05).

**Table 4**

**Characteristics of the correlations of prostatitis symptoms, depression and anxiety in patients with chronic calculous prostatitis before treatment (statistically significant Spearman correlation coefficients)**

<table>
<thead>
<tr>
<th>Indexes</th>
<th>NIH-CPSI Overall Score</th>
<th>NIH-CPSI pain domain</th>
<th>NIH-CPSI Dysuria domain</th>
<th>NIH-CPSI Quality of Life Domain</th>
<th>Erection IIEF</th>
<th>Orgasm IIEF</th>
<th>Libido IIEF</th>
<th>Satisfaction with coitus IIEF</th>
<th>Overall satisfaction IIEF</th>
<th>PHQ-9</th>
<th>GAD-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH-CPSI Overall Score</td>
<td>1.00</td>
<td>0.866</td>
<td>0.571</td>
<td>0.748</td>
<td>-0.785</td>
<td>-0.749</td>
<td>-0.782</td>
<td>-0.627</td>
<td>0.633</td>
<td>0.515</td>
<td></td>
</tr>
<tr>
<td>NIH-CPSI pain domain</td>
<td>0.866</td>
<td>1.00</td>
<td>0.224</td>
<td>0.613</td>
<td>-0.676</td>
<td>-0.631</td>
<td>-0.669</td>
<td>-0.565</td>
<td>-0.475</td>
<td>0.517</td>
<td>0.426</td>
</tr>
<tr>
<td>NIH-CPSI Dysuria Domain</td>
<td>0.571</td>
<td>0.224</td>
<td>1.00</td>
<td>0.142</td>
<td>-0.486</td>
<td>-0.553</td>
<td>-0.501</td>
<td>-0.516</td>
<td>-0.410</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NIH-CPSI Quality of Life Domain</td>
<td>0.748</td>
<td>0.613</td>
<td>0.142</td>
<td>1.00</td>
<td>-0.546</td>
<td>-0.442</td>
<td>-0.535</td>
<td>-0.438</td>
<td>-0.481</td>
<td>0.565</td>
<td>0.472</td>
</tr>
<tr>
<td>Erection IIEF</td>
<td>-0.785</td>
<td>-0.676</td>
<td>-0.486</td>
<td>-0.546</td>
<td>1.00</td>
<td>0.833</td>
<td>0.933</td>
<td>0.926</td>
<td>0.701</td>
<td>-0.474</td>
<td>-</td>
</tr>
<tr>
<td>Orgasm IIEF</td>
<td>-0.749</td>
<td>-0.631</td>
<td>-0.553</td>
<td>-0.442</td>
<td>0.833</td>
<td>1.00</td>
<td>0.896</td>
<td>0.846</td>
<td>0.638</td>
<td>-0.416</td>
<td>-0.340</td>
</tr>
<tr>
<td>Libido IIEF</td>
<td>-0.782</td>
<td>-0.669</td>
<td>-0.501</td>
<td>-0.535</td>
<td>0.933</td>
<td>0.896</td>
<td>1.00</td>
<td>0.909</td>
<td>0.685</td>
<td>-0.519</td>
<td>-0.424</td>
</tr>
<tr>
<td>Coitus satisfaction IIEF</td>
<td>-0.703</td>
<td>-0.565</td>
<td>-0.516</td>
<td>-0.438</td>
<td>0.926</td>
<td>0.846</td>
<td>0.909</td>
<td>1.00</td>
<td>0.773</td>
<td>-0.358</td>
<td>-</td>
</tr>
<tr>
<td>Overall satisfaction IIEF</td>
<td>-0.627</td>
<td>-0.475</td>
<td>-0.410</td>
<td>-0.481</td>
<td>0.701</td>
<td>0.638</td>
<td>0.685</td>
<td>0.773</td>
<td>1.00</td>
<td>-0.347</td>
<td>-</td>
</tr>
<tr>
<td>PHQ-9</td>
<td>0.633</td>
<td>0.517</td>
<td>-</td>
<td>0.565</td>
<td>-0.474</td>
<td>-0.416</td>
<td>-0.519</td>
<td>-0.358</td>
<td>-0.347</td>
<td>1.00</td>
<td>0.889</td>
</tr>
<tr>
<td>GAD-7</td>
<td>0.515</td>
<td>0.428</td>
<td>-</td>
<td>0.472</td>
<td>-0.340</td>
<td>-0.424</td>
<td>-</td>
<td>-</td>
<td>0.889</td>
<td>1.00</td>
<td>-</td>
</tr>
</tbody>
</table>
No significant changes in the presence of echo-positive inclusions were detected, however, a decrease in the frequency of detection of a twinkling artifact was observed (McNemar’s test, \( p=0.016 \)), which, in our opinion, indicates a decrease in the density of prostate calcification. Before treatment, a significant correlation of the presence of twinkling artifact was found with the total score of prostatitis symptoms (\( r = 0.448, p=0.005 \)), domains of pain (\( r = 0.404, p=0.013 \)) and quality of life (\( r = 0.331, p=0.045 \)), orgasm (\( r = -0.469, p=0.003 \)), libido (\( r = -0.350, p=0.034 \)). No correlation was found with other investigated indicators.

Previously, in the study of the success of the use of ESWT in calculous prostatitis at the State Institution «Acad. Of Vozianov Institute of Urology of the National Academy of Medical Sciences of Ukraine» clinical efficiency of 86.7% was achieved [12]. However, the dynamics of ejaculate interleukin levels were not investigated, and the ultrasonographic characterization of the prostate parenchyma did not include the definition of a twinkling artifact.

Other researchers, along with the good safety of the procedure, have shown a significant and long-lasting reduction in the activity of prostatitis symptoms, improvement in sexual function and quality of life when using ESWT in chronic prostatitis/chronic pelvic pain syndrome [13–16]. However, these studies did not examine immune and Doppler ultrasound correlates of disease symptoms.

In our study, the safety of the treatment was also good. Serious side effects were not identified. At the beginning of the treatment during the procedure, all patients experienced mild or moderate short-term (within a few seconds) pain in the projection of the prostate gland with irradiation in the perineum and/or coccyx. The intensity of unpleasant sensations decreased after 5-7 ESWT procedures.

We consider the limitations of our study:
- a small number of observations;
- lack of generally recognized objective criteria for the diagnosis of «Chronic calculous prostatitis», which is also considered as chronic bacterial prostatitis or CP/CPPS in combination with prostate stones;
- lack of control of treatment results in the form of a false procedure.

**CONCLUSIONS**

Extracorporeal shock wave therapy has an anti-inflammatory and analgesic effect, provides a significant reduction in prostatitis symptoms, comorbid symptoms of depression, anxiety and sexual dysfunction. It is a safe and quite effective means of treatment of chronic prostatitis / chronic pelvic pain syndrome. Clinically significant improvement was achieved in 72.9% of patients.

Twinkling artifact is an important ultrasonographic phenomenon that can be used to characterize prostate calcifications and monitor their changes during treatment.
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