CLINICAL STUDY REPORT

TITLE PAGE

Study Title	Evaluation of SWT (BTL-6000 SWT) efficiency in alleviation of chronic prostate inflammation
Name of the Investigational Product	BTL-6000 SWT
Indication for Use	Shock Wave Therapy device (BTL-6000 SWT) is intended for treatment of patients with symptoms of chronic pelvic pain syndrome (CPPS).
Sponsor	BTL Industries Ltd 30 Peshtersko Shouse Blvd Plovdiv 4002, Bulgaria
Protocol	Version 100: 25.10.2013
Study Initiation Date	January 2014
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Evaluation of SWT (BTL-6000 SWT) efficiency in alleviation of chronic prostate inflammation

ABSTRACT

Purpose & Primary Objective:

This study was designed to investigate the effectiveness of extracorporeal shock wave therapy (ESWT) for symptoms alleviation in patients with chronic pelvic pain syndrome (CPPS).

The primary efficacy outcome is set to be a minimum of 50% of symptom alleviation in 50% of subjects after the last treatment with results lasting at the same level or being deteriorated by ≤10% at 90-day follow up.

Methods:

Twenty nine male subjects of 27-70 years of age who suffering from chronic pelvic pain for more than 3 months and having no addiction to drugs or narcotics. All subjects received 4 treatments over 4-week period, with BTL-6000 SWT unit.

Results:

All subjects completed the treatment and 30-day follow up. All but two subjects (105 and 207) completed 90-day follow up. After the last treatment, twenty four subjects (82,76%) showed ≥50% alleviation of the pelvic pain and urinary symptoms. Mean symptom alleviation through all 29 patients was 68%. Mean symptom alleviation after 30-day follow up showed result 73%. After 90-day follow up was mean symptom alleviation back at 68%.

According to the response of the treatment, patients could be divided into two groups. In one group pre- and post-treatment evaluations showed significant reduction of symptoms (≥50%), from moderate to mild on Symptom Scale Score (SSS), with difference 5-15 points of the SSS.

In the second group, three subjects had relief from severe to moderate symptoms (even though two subjects did not comply the symptom alleviation ≥50%).Yet even another three subjects had highly significant relief from severe to mild symptoms on SSS, with difference of 11-16 points of the SSS.

The BTL-6000 SWT subjects have met the primary efficacy outcome measure by achieving a minimum of 50% of symptom alleviation in 50% of subjects after the last treatment with results lasting at the same level or being deteriorated by ≤10% at 90-day follow up.

Conclusion:

BTL-6000 SWT subjects have met the primary efficacy outcome measure and the shockwave procedure produces consistent, significant symptom alleviation after 4 once-a-week treatments, immediately post-treatment and at 30-day and 90 day follow up.

The results of the study show that the ESWT device BTL-6000 SWT is safe and efficacious for reducing chronic pelvic pain and urinary symptoms. Patients tolerate the treatment sessions nicely.

I. INTRODUCTION

Extracorporeal shock wave therapy is non-invasive therapeutic device intended to be used in case of musculoskeletal system disorders. Application of shockwave energy into the tissue decreases pain sensations and supports local microcirculation what results in local metabolism enhancement.

BTL Industries Ltd. conducted their own evaluation of the BTL-6000 SWT device for alleviation of the symptoms of 29 patients suffering with chronic prostate inflammation, at a site in Clinic of urology to the „St.Anna“ University Hospital - Sofia, Bulgaria. We worked with the positive effect of shockwaves on local neovascularisation, reversal of chronic inflammation. These long-term mechanism are also supported with intense local vasodilatation and immediate pain suppression.

The device uses the ballistic principle of the shockwave generation. The shock wave is formed via a projectile by accelerated compressed air, which is generated by an electronically controlled air-compressor. The kinetic energy of the projectile is transferred into a probe of the applicator and subsequently into the client's body. During the treatment the ending part of the applicator must be in immediate contact with the skin and subcutaneous tissue.

II. MATERIALS AND METHODS

Design

Study Type: Interventional

Study Design:

- Endpoint Classification: Efficacy Study
- Primary Purpose: Treatment

The study evaluated the clinical improvement in pain and urinary symptoms in subjects suffering from chronic prostate inflammation by treatment with BTL-6000 SWT device (BTL Industries Ltd., Bulgaria).

The patients were examined prior to the first treatment, when symptom scale score (pain and urinary symptoms) and total scale score (pain, urinary and quality of life symptoms) were inquired. Symptom scale score and total scale score were evaluated according to The National Institutes of Health Chronic Prostatitis Symptoms Index (NIH-CPSI). NIH-CPSI provides a valid outcome measure for men with chronic prostatitis. The primary component is pain, captured in 4 items that focus on location, severity, and frequency. Urinary function, another important component of patients' symptoms is captured in 2

items - 1 irritative and 1 obstructive. Impact and overall quality of life are captured with 3 additional items that ask about the effect of symptoms on daily activities. The 9 items have high test-retest reliability (r=0.86-0.92) and internal consistency (r=0.82-0.91). "Symptom scale score" (SSS) - calculate and report the pain and urinary score (range 0-31): mild =0-9; moderate=10-18; severe=19-31. "Total score" - calculate and report total score (range 0-43).

After informed consent was obtained each subject received 4 SWT treatments at weekly intervals with a standard treatment procedure. Patients were examined prior to the first treatment, after the last treatment, with 30-days and 90-days follow-up.

Sites & Subjects

The study enrolled 29 subjects at one investigation site: Clinic of urology to the „St.Anna“ University Hospital - Sofia, Bulgaria

Primary Outcome Measures

The primary efficacy outcome is set to be a minimum of 50% of symptom alleviation in 50% of subjects after the last treatment with results lasting at the same level or being deteriorated by ≤10% at 90-day follow up.

Inclusion Criteria

- chronic pelvic pain existence for more than 3 months
- certain diagnosis of chronic nonbacterial/chronic pelvic pain syndrome defined as pain in the bladder, groin, genitalia or lower abdomen
- non-addiction to drugs and narcotics

Exclusion Criteria

- other pathologies
- evidence of bacterial in urinary and seminal culture tests (criteria according NIH classification)

Treatment Procedure

The therapy was administered in contact manner using direct application above the target area.

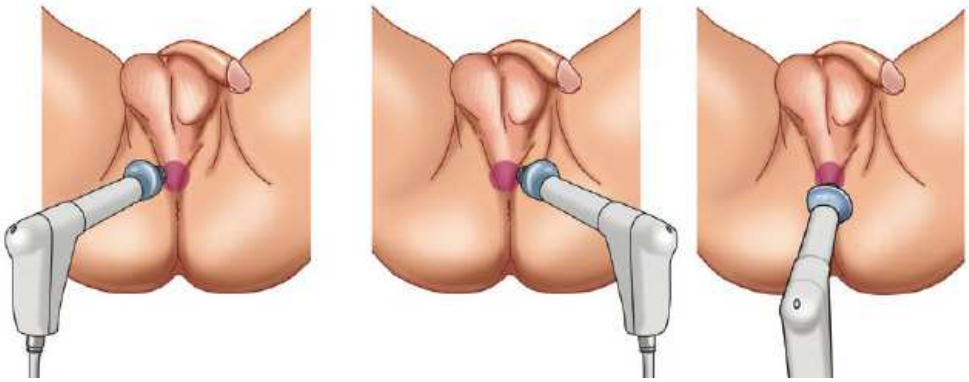
The application pressure was set to 3 bars and frequency to 8 Hz. If the therapy was well tolerated, the pressure was progressively increased up to 5 bars. The therapy pressure was always adjusted based on the feedback from the patient. The therapy might be intense but not painful.

First 500 pulses were applied with the applicator positioned with approximately 30° angle deviation to the left side. Next 500 pulses were applied on opposite 30° angle deviation to the right side. Last 1500 pulses were applied in the central position of the applicator (see Picture 1). Horizontal position of the applicator remains unchanged throughout the entire treatment.

Treated Area

Subjects were treated with ergonomic applicator (see Picture 1).

Picture 1.



Data analysis

Pain, urinary and quality of life symptoms were investigated:

- Before the first treatment
- After the last (fourth) treatment
- At 30-day follow up visit
- At 90-day follow up visit

III. RESULTS

Subjects' age ranged from 27 to 70 years with the mean age of 42.51 ± 12.05years. All subjects in the study received 4 weekly treatments.

The treatment was well tolerated. Initial pressure was set at 3 bars, progressively increased up to 5 bars, if tolerated.

Symptom Scale Score

Table 1 – BTL-6000 SWT Treatment Group – Alleviation of pain and urinary symptoms

#	Patient No	Age	Alleviation of symptoms %		
			Alleviation of symptoms - After last treatment	Alleviation of symptoms - After 30-dayFollow Up	Alleviation of symptoms - After 90-dayFollow Up
1	101	33	93%	93%	93%
2	102	56	75%	81%	75%
3	103	54	81%	81%	81%
4	104	60	62%	71%	62%
5	105	50	83%	92%	N/A
6	106	46	81%	88%	81%
7	107	66	54%	58%	54%
8	108	70	85%	85%	85%
9	109	64	48%	59%	59%
10	110	41	48%	61%	52%
11	111	40	80%	85%	80%
12	112	45	85%	85%	85%
13	113	46	56%	56%	50%
14	114	37	86%	86%	86%
15	115	49	83%	89%	83%
16	116	51	36%	36%	36%
17	201	36	77%	85%	85%
18	202	27	58%	68%	63%
19	203	31	25%	25%	25%
20	204	32	83%	83%	83%
21	205	30	77%	85%	85%
22	206	35	67%	67%	61%
23	207	32	75%	88%	N/A
24	208	35	76%	82%	76%
25	209	33	50%	60%	60%
26	210	30	56%	67%	67%
27	211	37	36%	36%	36%
28	212	33	83%	83%	83%
29	213	34	69%	69%	54%

Table 2 – BTL-6000 SWT Treatment Group – Mean Alleviation of Symptoms

		Mean Alleviation of symptoms (%)		
	Age	Alleviation of symptoms - After last treatment	Alleviation of symptoms - After 30-dayFollow Up	Alleviation of symptoms - After 90-dayFollow Up
Mean±**SD**	42,51±12,05	68% ±17,8%	73% ±17,87%	68% ±18,08%

Table 3 – BTL-6000 SWT Treatment Group – Symptom Scale Scores and Difference of Symptom Scale Score Points

#	Patient No	Age	**Symptom scale scores (SSS)**				**Difference of SSS points**		
			SSS – Before the first treatment (range 0-31)	SSS – After the last treatment (range 0-31)	SSS - After 30-day follow up (range 0-31)	SSS - After 90-day follow up (range 0-31)	Before Tr./After last Tr.	Before Tr./After 30-day FU	Before Tr./After 90-day FU
1	101	33	14	1	1	1	13	13	13
2	102	56	16	4	3	4	12	13	12
3	103	54	16	3	3	3	13	13	13
4	104	60	21	8	6	8	13	15	13
5	105	50	12	2	1	N/A	10	11	N/A
6	106	46	16	3	2	3	13	14	13
7	107	66	24	11	10	11	13	14	13
8	108	70	13	2	2	2	11	11	11
9	109	64	27	14	11	11	13	16	16
10	110	41	23	12	9	11	11	14	12
11	111	40	20	4	3	4	16	17	16
12	112	45	13	2	2	2	11	11	11
13	113	46	16	7	7	8	9	9	8
14	114	37	14	2	2	2	12	12	12
15	115	49	18	3	2	3	15	16	15
16	116	51	11	7	7	7	4	4	4
17	201	36	13	3	2	2	10	11	11
18	202	27	19	8	6	7	11	13	12
19	203	31	8	6	6	6	2	2	2
20	204	32	12	2	2	2	10	10	10
21	205	30	13	3	2	2	10	11	11
22	206	35	18	6	6	7	12	12	11
23	207	32	8	2	1	N/A	6	7	N/A
24	208	35	17	4	3	4	13	14	13
25	209	33	10	5	4	4	5	6	6
26	210	30	9	4	3	3	5	6	6
27	211	37	11	7	7	7	4	4	4
28	212	33	6	1	1	1	5	5	5
29	213	34	13	4	4	6	9	9	7

Table 4 – BTL-6000 SWT Treatment Group – Mean Symptom Scale Scores and Mean Difference of Symptom Scale Score Points

		Mean Symptom Scale Score (range 0-31)				Mean Difference of SSS Points		
	Age	SSS – Before the first treatment	SSS – After the last treatment	SSS - After 30-day follow up	SSS - After 90-day follow up	Before Tr./After last Tr.	Before Tr./After 30-day FU	Before Tr./After 90-day FU
Mean ±SD	42,51 ±12.05	14,86±5,01	4,83±3,32	4,07±2,84	4,85±3,10	10,03 ±3,63	10,79 ±3,99	10,37 ±3,79

Quality of life (QOL) score

Table 5 – BTL-6000 SWT Treatment Group – Mean Quality of life Score and Mean Improvement in QOL points (%)

		Mean Quality of life Score				Mean Improvement in QOL points (%)		
	Age	Before the first treatment	After the last treatment	After 30-day follow up	After 90-day follow up	Before Tr./After last Tr.	Before Tr./After 30-day FU	Before Tr./After 90-day FU
Mean ±SD	42,51±12, 05	7,55±2,56	1,62±1,76	1,38±1,47	1,63±1,62	77,63% ±25,11%	80,37% ±22,61%	76,99% ±24,78%

Table 6– BTL-6000 SWT Treatment Group – Mean Total Score and Mean Improvement in Total score points (%)

		Mean Total Score				Mean Improvement in Total score points (%)		
	Age	Before the first treatment	After the last treatment	After 30-day follow up	After 90-day follow up	Before Tr./After last Tr.	Before Tr./After 30-day FU	Before Tr./After 90-day FU
Mean ±SD	42,51± 12,05	22,41±7,3	6,45±4,59	5,45 ±3,93	6,48 ±4,26	71,26% ±18,97%	75,23% ±18,38%	71,23% ±18,78%

Pre-Treatment vs. Post-Treatment Evaluation

BTL-6000 SWT Treatment Group. The treatment group subjects showed an average of 68±17,8% alleviation of pain and urinary symptoms after the last treatment (Table 2).

Mean difference of symptom scale score points before treatment and after the last treatment results was 10,03±3,63 (Table 4).

First group of 19 patients showed significant reduction of symptoms from moderate to mild on Symptom Scale Score (SSS) (average 73%,), with difference 5-15 points of the SSS. The second group of patients includes three subjects (#107, 109 and 110) who had relief from severe to moderate symptoms (even though two subjects did not comply with the symptom alleviation ≥50%). Another three subjects (#104, 111 and 202) had even relief from severe to mild symptoms on SSS, with difference of 11-16 points of the SSS (See table 3). 4 patients (#203, 207, 210 and 212) stayed at the level of mild symptoms, though there was improvement in their SSS (2-6 points) (See table 3).

The post-treatment evaluation showed mean improvement in Quality of life points with 77,63±25,11% and Total score with 71,26±18,97%. (See Table 5, Table 6)

Pre-Treatment vs. 30-day Follow up Evaluation

BTL-6000 SWT Treatment Group. The treatment group of 29 subjects showed an average of 73±17,87 % alleviation of pain and urinary symptoms after 30-day follow up (Table 2). There were 26 (89%) subjects with ≥50% alleviation of symptoms (Table 1).

Mean difference of symptom scale score points before treatment and after 30-day follow up was 10,79±3,99 (Table 4).

The first group of 19 patients (reduction of symptoms from moderate to mild) achieved even 76% alleviation of symptoms. 1 patient (#110) got improved from severe to mild symptoms at 30 days Follow up. 2patients (#107, 109) stayed at the level of moderate symptoms. (See table 3).

Mean improvement in Quality of life points of the treatment group was 80,37±22,61% and respectively in the Total scores 75,23±18,38%. (See Table 5, Table 6)

Pre-Treatment vs. 90-day Follow up Evaluation

BTL-6000 SWT Treatment Group. Two subjects (#105 and 207) did not complete the 90-day follow up. The treatment group of 27 patients showed an average of 68±18,08 % alleviation of pain and urinary symptoms after 90-day follow up (Table 2). There were 24 (88,89%) subjects with ≥50% alleviation of symptoms (Table 1).

Mean difference of symptom scale score points before treatment and after 90-day follow up was 10,37±3,79 (Table 4).

The first group of patients (reduction of symptoms from moderate to mild) achieved 72% alleviation of symptoms. Patient #110 got back to the results comparable to after treatment state- from severe to moderate; two subjects (#107, 109) had relief from severe to moderate symptoms also; another three subjects (#104, 111 and 202) had significant relief from severe to mild symptoms on SSS (See table 3). Patients #203, 210 and 212 stayed at the level of mild symptoms but still with Mean Alleviation of Symptoms58%.

At 90-day Follow-up evaluation reported Mean improvement in Quality of life was 76,99±24,78% and 71,23±18,78% in Total score. (See Table 5, Table 6)

Adverse Events

There was not reported any adverse event.

IV. DISCUSSIONS

The benign hyperplasia of the prostate is one of the most common urogenital diseases in men. Chronic pelvic pain syndrome (CPPS) is connected to symptoms affecting the quality of everyday life, as pain, urinary problems and others. There is a well-founded demand for effective non-invasive solution of the problems, as extracorporeal shock wave therapy (ESWT).

In this study, 29 subjects were treated with the BTL-6000 SWT to achieve alleviation of the symptoms of chronic pelvic pain syndrome (CPPS). The treatment efficacy was assessed by comparing pre-treatment Symptom Scale Scores (pain and urinary symptoms), 30-day and 90-day follow up SSS, performed by an independent, experienced evaluator.

To meet the primary efficacy outcome measure the subjects from the BTL-6000 SWT Treatment Group had to demonstrate that minimum of 50% of subjects had symptom alleviation of 50% after the last treatment and results lasting at the same level or being deteriorated by ≤10% at 90-day follow up.

At post-treatment evaluation point the mean alleviation of pain and urinary symptoms was 68±17,8 %; 73±17,87 % after 30-day Follow up and 68±18,08 % after 90-day Follow up at the end of the study. The BTL-6000 SWT Treatment group met the primary efficacy outcome.

All scores decreased over the post-treatment and follow up period, the NIH-CPSI total, pain, and quality of life scores were significantly improved in the whole treatment group. All patients tolerated procedures well with no significant post-treatment pain or clinical signs of skin damage.

Two patients did not accomplish the 90-day follow up.

V. CONCLUSIONS

The BTL-6000 SWT subjects have met the primary efficacy outcome measure by achieving a minimum of 50% of symptom alleviation in 50% of subjects after the last treatment with results lasting at the same level or being deteriorated by ≤10% at 90-day follow up.

BTL-6000 SWT produces consistent, statistically significant alleviation of symptoms of chronic pelvic pain syndrome in 4 once-a-week treatments, immediately post-treatment and at 30-day and 90-day follow up.

There was statistically significant difference in:

- Pain and urinary symptoms values before the treatment and after the last treatment
- Pain and urinary symptoms values before the treatment and after the 30-day follow up
- Pain and urinary symptoms values before the treatment and after the 90-day follow up

The 4 weekly treatments with BTL-6000 SWT produce reliable alleviation of symptoms of chronic pelvic pain syndrome.