CLINICAL STUDY REPORT

TITLE PAGE

Study Title	Evaluation of SWT efficiency in treatment of Erectile Dysfunction
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 in treatment of erectile dysfunction (ED).
Sponsor	BTL Industries Ltd 30 Peshtersko Shouse Blvd Plovdiv 4002, Bulgaria
Protocol	
Study Initiation Date	January 2014
Study Completion Date	April 2014
Date of Report	20.5.2014
Principal Investigator(s) and Sites	Assoc. Prof. Krasimira Kazalakova, MD, Head of Physiotherapy and rehabilitation ward in University Multiprofile Hospital for Active Treatment and Emergency Medicine „N. I. Pirogov“, Sofia, Bulgaria
Sponsor Contact	Georgi Petkov BTL Industries Ltd 30 Peshtersko Shouse Blvd Plovdiv 4002, Bulgaria +359 32 622 252 petkov@btl.bg

Evaluation of SWT efficiency in treatment of Erectile Dysfunction

ABSTRACT

Purpose & Primary Objective:

The main objective of the study was to investigate and prove the effectiveness and safety of extracorporeal shock wave therapy (ESWT) in treatment of erectile dysfunction (ED) caused by vascular disorders.
The primary efficacy outcome is set to be a minimum increase in IIEF-EF ≥ 5 points in 50% of subjects after the last treatment with results lasting a at the same level at 90-day follow up.

Materials and Methods:

We treated 8 middle-aged men 48-65 years old (average age: 55.5 ± 6.3 yr) with vasculogenic ED existence for more than 6 months. Patients underwent 8 treatments on every 3 - 4 days with BTL-6000 SWTunit.
Assessment of erectile function was performed at screening, after the last treatment and at the 3- and 6-month follow-up examinations using the International Index of Erectile Function (IIEF) questionnaire. Outcome measures used are changes in the International Index of Erectile Function-erectile function domain (IIEF-EF) scores. Safety assessment was based on complications and reported adverse events.

Results:

All patients completed the treatment protocol of 8 consecutive procedures, 30 and 90-day follow-up visits.Pre- and post-treatment collected parameters from 5 patients (62.5%) met the primary efficacy criteria of IIEF-EF increase ≥ 5 points.). At 90 day follow-up examination, the IIEF-EF scores remained at the same level.

Conclusion:

The main object of the study was to investigate the effectiveness and safety of extracorporeal shock wave therapy (ESWT) in treatment of erectile dysfunction (ED) caused by vascular disorders. The results of the study show that the ESWT device BTL-6000 SWT is safe and efficacious to improve erectile function. Patients tolerate the treatment sessions well.

I. INTRODUCTION

Erectile dysfunction (ED) is a common problem which affects large population of men especially in 40-70 years of age. The most common cause of erectile dysfunction is poor cavernosal arterial blood flow in the penis - vasculogenic ED. The current nonsurgical treatment options for erectile dysfunction mainly consist of oral phosphodiesterase type 5 inhibitors (PDE5is) and/or intracavernosal injections of vasodilating agents. But these treatments do not affect the underlying pathophysiology of the erectile mechanism, their effect is time limited.
Shockwave therapy is a non-invasive, non-pharmacological therapy which triggers a natural mechanism in treated area. ESWT induces cellular microtrauma, which in turn stimulates the release of angiogenic factors and the subsequent neovascularization of the treated tissue. The study aimed to prove that inducing neovascularization by extracorporeal shock wave therapy could potentially improve cavernosal arterial flow which will lead to improved erectile function and may allow restoration of penile function and sexual spontaneity
BTL-6000 SWT is a radial shockwave therapy device enabling the application of therapy by using handheld pneumatic applicator.

II. MATERIALS AND METHODS

Design

Study Type: Interventional

Study Design:
Endpoint Classification: Efficacy Study
Primary Purpose: Treatment

This is a prospective single/center, open label clinical study of the Shock Wave device intended for treatment the patients with symptoms of erectile dysfunction (ED) caused by vascular disorders. The clinical improvement in erectile function was evaluated after treatment with BTL-6000 SWT device (BTL Industries Ltd.).
The International Index of Erectile Function (IIEF) was used as a diagnostic tool for the evaluation of male sexual function. Each patient completed the validated questionnaires before the first treatment, after the last treatment and at the follow-up visits. It consists of five domains of erectile function: six questions about erectile function, two about orgasmic function, two about sexual drive, three about intercourse satisfaction, and two about overall satisfaction.

Safety assessments were based on complications and reported adverse events.

After informed consent was obtained patients underwent 8 treatments on every 3 – 4 days. Patients were examined before first treatment, after the last treatment, with 30-days and 90-days follow-up visits.

Sites & Subjects

The study enrolled 8 subjects at one investigation site: University Multiprofile Hospital for Active Treatment and Emergency Medicine „N. I. Pirogov“, Sofia, Bulgaria

Primary Outcome Measures

Outcome measures used are changes in the International Index of Erectile Function-erectile function domain (IIEF-EF) scores. The primary efficacy outcome is set to be a minimum increase in IIEF-EF ≥ 5 points in 50% of subjects after the last treatment with results lasting a at the same level at 90-day follow up.

Secondary Outcome Measures:

Safety assessment was based on complications and reported adverse events.

Inclusion Criteria

- Erectile dysfunction existence for more than 6 months
- Metabolic syndrome
- Hypertension
- Diabetes
- Normal level of testosterone

Exclusion Criteria

- other pathologies

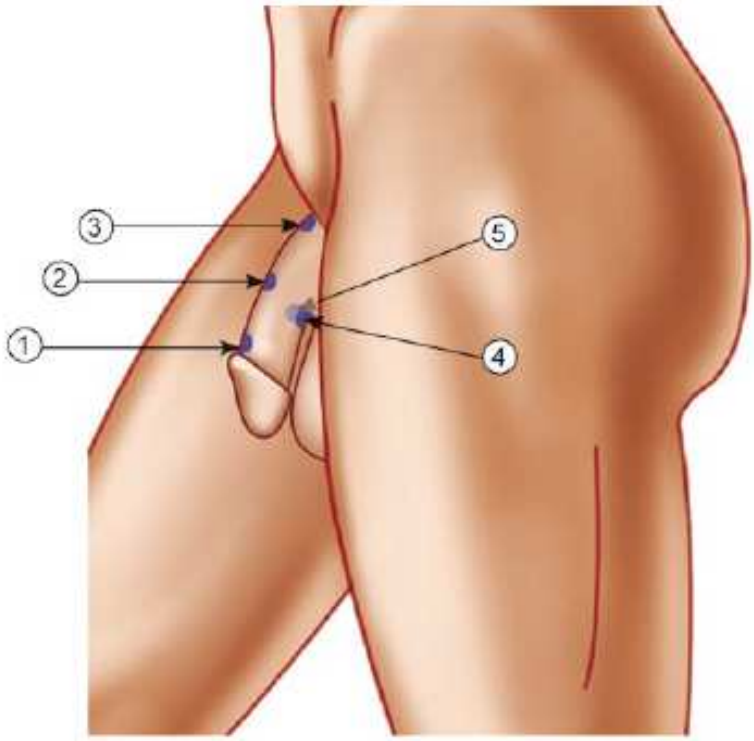
Treatment Procedure

The therapy was performed in 5 consequent steps/areas with 600 pulses applied in each step/area using static application. (Pic.1) Starting from the first therapy session the total number of the pulses was 3000 per one session.
The application pressure was set to 1,5 bar and frequency to 12 Hz. If the therapy was well tolerated, the pressure was progressively increased up to 2 bars. The therapy was administered in contact manner using direct application above the target area.

Treated Area

The area was treated with handheld pneumatic applicator. (Pic. 1). The shockwaves were applied to the distal, mid and proximal penile shaft, left and right crura.

Picture 1.



Data analysis

The International Index of Erectile Function (IIEF) domain scores were analysed:

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

III. RESULTS

Eight middle-aged men with vasculogenic ED completed the treatment protocol of 8 consecutive procedures. All patients accomplished the 30 and 90-day follow-up visits. The subject's age ranged 48-65 years (mean 55.5 ± 6.3 yr).

Table 1 displays the calculated IIEF-EF domain score of each study participiant from baseline to 90 day after the end of treatment. The mean results from IIEF domains (erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction) are presented in Tabel 2. Table 3 summarizes total IIEF improvement after the last treatment procedure, at 30 and 90 day follow-up compared to the baseline.

Table 1. IIEF-EF domain score of each study participiant from baseline to 90 day after the end of treatment

Patient	Age	IIEF-EF Baseline	IIEF-EF Post-treatment	IIEF-EF at 30 day	IIEF-EF at 90 day	Δ IIEF-EF Baseline/ post-treatment	Δ IIEF-EF Baseline/ 30 day	Δ IIEF-EF Baseline/ 90 day
101	49	12	25	25	25	13	13	13
102	50	12	12	13	13	0	1	1
103	62	16	25	25	25	9	9	9
104	65	23	25	26	25	2	3	2
105	60	11	21	21	21	10	10	10
106	56	6	18	18	19	12	12	13
107	54	18	24	24	24	6	6	6
108	48	23	25	25	26	2	2	3

Table 2. Results from mean IIEF domains before and 90 day after after the end of treatment

Domains scores	Mean Baseline score ± SD	Mean Post-treatment score ± SD	Mean 30 day F/U score ± SD	Mean 90 day F/U score ± SD
Erectile Function	15.12 ± 6.01	21.87 ± 4.73	22.13 ± 4.55	22.25 ± 4.43
Orgasmic Function	5.12 ± 2.23	8.12 ± 2.17	8.38 ± 1.99	8.38 ± 1.99
Sexual Desire	5.37 ± 1.6	7.87 ± 0.99	8 ± 1.07	8 ± 1.07
Intercourse Satisfaction	7.87 ± 3.18	12.25 ± 2.55	12.25 ± 2.54	12.25 ± 2.55
Overall Satisfaction	3.75 ± 2.19	7.5 ± 1.69	7.5 ± 1.69	7.62 ± 1.77

Table 3. Improvement in Total IIEF from baseline to 90 day follow-up

Total IIEF	Baseline/ post-treatment	Baseline/ 30 day F/U	Baseline/ 90 day F/U
% improvement	55.03%	56.38%	57.05%

Pre- and post-treatment collected parameters from 5 patients (62.5%) met the primary efficacy criteria of IIEF-EF increase ≥ 5 points. A significant improvement, more than 10 points, in IIEF-EF domain score was noted in 3 patients (101,105 and 106). Three patients recorded improvent in EF with <10 points. No changes in IIEF-EF were measured only in one patient (102). At the 30 day and 90 day follow-up examinations, the IIEF-EF scores remained at the same level. Three of the patients (102, 104, 106) had an increase of one point in the EF domain. (see Table 1)

All domains scores were high after the treatment and at follow-up examinations. Mean post-treatment EF was 21.87 ± 4.73 compared to the baseline 15.12 ± 6.01. Orgasmic function, sexual desire and intercourse satisfaction improved sigfnificantly, but overall satisfaction mean scores were with the highest improvement 3.75 ± 2.19 vs. 7.5 ± 1.69 after the treatment. These results were maintained and even slight rise was observed at 30 and 90 days follow-up examinations. (see Table 2)

The calculated improvement in total IIEF after the last treatment was 55.03% and reached 57.05% at 90 day follow-up.

No adverse events were reported during the sessions and follow-ups. Patient tolerance of the treatments was excellent, none of the subjects reported treatment-associated pain during or after the treatment.

IV. DISCUSSION

A variety of treatments are now available for men with erectile dysfunction (ED). Phosphodiesterase type 5 inhibitors (PDE5Is) are a most popular treatment option, but have been marketed, that they cannot restore pathological changes in the penis. Extracorporeal shock wave therapy (ESWT) is a novel modality that has recently been developed for treating ED. It aims to restore the erectile mechanism in order to enable natural or spontaneous erections, as opposed to traditional treatments all of which are designed to attenuate symptoms.

The first study, that proved the efficacy of low-energy shock wave therapy (LESWT) for ED was conducted by Vardi et al. in 2010. Animal studies have shown also that LESWT significantly improves penile hemodynamics and restores pathological changes in the penis of diabetic ED animal models. Further clinical studies also showed satisfactory feasibility of shockwave procedures as well of males who responded to PDE5I and in patients responded poorly to PDE5I therapy.
Although, still limited number of patients, our results demonstrate that ESWT has a genuine physiological effect on the erectile mechanism. 62.5% met the primary efficacy criteria of IIEF-EF increase ≥ 5 points. However, further extensive clinical studies are needed.

V. CONCLUSIONS

The mainobject of the study was to investigate the effectiveness and safety of extracorporeal shock wave therapy (ESWT) in treatment of erectile dysfunction (ED) caused by vascular disorders. The results of the study show that the ESWT device BTL-6000 SWT is safe and efficacious to improve erectile function. Patients tolerate the treatment sessions well. A significant increase in the duration of erection and penile rigidity were reported. It was observed a genuine physiological and psychological effect on the erectile mechanism
ESWT is a new treatment option for erectile dysfunction, enabling the patient to achieve and maintain dependable erections.