

Penile low intensity shock wave therapy for PDE5i non-responders suffering from vasculogenic Erectile Dysfunction since 2 to 10 years: A prospective, randomized, placebo-controlled study (2016)

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Background: Several animal and human studies have evaluated the role of low-intensity extracorporeal shockwave therapy (LIST) in the management of multiple disorders such as chronic wounds, peripheral neuropathy and cardiac ischemic disease. LIST was reported to trigger a chain of events that releases angiogenic factors, recruits endothelial progenitor cells, induces neovascularization and enhances blood flow in treated areas. Recently, some studies with contradictory results have assessed the efficacy and safety of this therapy on patients suffering erectile dysfunction.

Aim: Investigate the effects of penile LIST on erectile function in long-term patients suffering from erectile dysfunction since 2-10 years and are refractory to phosphodiesterase type 5 inhibitors (PDE5i).

Methods: Prospective, randomized, simple-blind, sham-controlled study. In total 58 patients with vasculogenic erectile dysfunction refractory to PDE5i were randomized into two groups. 30 were treated with electrohydraulic low intensity shock waves (1 session/week for 6 weeks; 1,500 pulses of 0.10 mJ/mm² at 5 Hz, urogold100® MTS) and 28 were treated with a sham probe. Eleven patients withdrew from the study and were lost to follow-up. All patients were evaluated at baseline and 1 month after the end of treatment using validated erectile dysfunction questionnaires like the International Index of Erectile Function (IIEF-5) and the Sexual Encounter Profile (SEP). Demographic and clinical characteristics were recorded. Data analysis investigated specifically the long-term patients suffering from ED since 2-10 years, which were in total forty-one patients; 22 in the verum group, 19 in the sham group.

Results: 22 active-treated patients and 19 sham-treated patients, suffering from ED since 2-10 years were analyzed. There was no significant difference between the two groups in baseline characteristics. Baseline five-item version of the IIEF-5 mean scores, in the active and sham groups, were 10.0 ± 4 and 9.9 ± 4.6, respectively (p= 0.94). At baseline, 14% of patients in the active group (3 of 22) and 10.5% of patients in the placebo group (2 of 19) had a positive answer to the SEP 3 question (p= 0.8). One month after treatment IIEF-5 scores mean changes from baseline, in the active and placebo group, were 2.2 ± 4.9 and 0.25 ± 4.4, respectively (p= 0.2). SEP 3 positive responders increased by 33% in the active group (7 of 22) and even decreased in the placebo group to 5% (1 of 19) (p=0.03) after LIST.

Conclusion: In this prospective study, 1 month of moderate LIST treatment led to partial recovery of erectile function at one-month follow up, as the amount of positive SEP3 responders significantly

increased 4 times and the average IIEF-5 score improved 8 times in the active group compared to the sham control group which, showed no placebo-effect. More studies with larger sample size and longer follow-up, comparing different lithotripters and shock wave protocols, are imperative to define alternative protocols and the role of LIST in erectile dysfunction for long term ED patients.

Baseline characteristics and statistical outcome of patients with 2-10 years ED

| | Active group | Sham group | p-value (unpaired, two-tailed student's t-test) |
|--|----------------|----------------|---|
| No. patients | 22 | 19 | |
| Median age (years, mean \pm SD) | 62.7 \pm 6.5 | 58.8 \pm 7.9 | 0.1 |
| ED duration (years, mean \pm SD) | 4.6 \pm 2.9 | 5.5 \pm 2.6 | 0.29 |
| Patients with cardiovascular risk factors (%) | 19 (86%) | 14 (74%) | 0.32 |
| Median IIEF-ED score baseline (mean \pm SD) | 10 \pm 4.0 | 9.9 \pm 4.6 | 0.94 |
| Median IIEF-ED score after treatment (mean \pm SD) | 12.2 \pm 6.1 | 10.2 \pm 4.7 | 0.25 |
| Median IIEF-ED score difference (after treatment - baseline) (mean \pm SD) | 2.2 \pm 4.9 | 0.26 \pm 4.4 | 0.2 |
| Positive SEP-3 (%) baseline | 3 (14%) | 2 (10.5%) | 0.8 |
| Positive SEP-3 (%) after treatment | 7 (32%) | 1 (5%) | 0.03 |
| Positive SEP-3 (%) difference (after treatment - baseline) | 4 (18%) | -1 (0%) | 0.94 |

Summary outcome of patients with 2-10 years ED:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
 - Sham group: 0, (n = 19)
 - Active group: 4, (n = 21)**→ SEP-3 increase of 400% vs. control**
4-times more positive upon LIST compared to the control group.
2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
 - Sham group: 0.26
 - Active group: 2.2**→ IIEF-ED score increase of 829% vs. control**
8.3-times better score in average compared to the control group.

Summary outcome of all patients that were analyzed:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
 - Sham group: 1, (n = 20)
 - Active group: 5, (n = 27)**→ SEP-3 increase of 500% vs. control**
5-times more positive upon LIST compared to the control group.
2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
 - Sham group: 0.5
 - Active group: 1.6**→ IIEF-ED score increase of 319% vs. control**
3.2-times better score in average compared to the control group.

Summary outcome of patients with cardiovascular risk factors (ischemic heart disease/hypertension/dislipemia) but NO diabetes mellitus:

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
 - Sham group: 1, (n = 12)
 - Active group: 5, (n = 16)**→ SEP-3 increase of 500% vs. control**
5-times more positive upon LIST compared to the control group.
2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
 - Sham group: -0.7
 - Active group: 1.8**→ IIEF-ED score increase of 180% vs. control**
1.8-times better score in average compared to the control group.

Summary outcome of patients WITH diabetes mellitus AND cardiovascular risk factors (ischemic heart disease/hypertension/dislipemia):

1. **SEP-3:** Number of patients who turned from negative into positive SEP-3 response upon 1 month of LIST treatment:
 - Sham group: 0, (n = 8)
 - Active group: 0, (n = 11)

→ **no difference between treatment and control**
2. **IIEF-ED:** Average improvement of the IIEF score upon 1 month of LIST:
 - Sham group: 2.3
 - Active group: 1.3

→ **SEP3 decrease of 43.3% vs. control**

Patients suffering from diabetes mellitus did not respond to LIST treatment in this study.

ED: Erectile Dysfunction

IIEF-ED: International Index of Erectile Dysfunction – erectile function domain

LIST: Low-Intensity Extracorporeal Shockwave Therapy

SD: Standard Deviation

SEP: Sexual Encounter Profile question 3: *Did your erection last long enough for you to have successful intercourse?*