Original Article

Efficacy of Low-Intensity Extra Corporal Shockwave Therapy (LI-ESWT) in Patients With Erectile Dysfunction

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Abstract

Objective: Erectile dysfunction (ED) is a common cause of sexual disorders in men with limited treatment options. This study aimed to determine the efficacy of low-intensity extra corporal shockwave therapy (LI-ESWT) in patients suffering from ED.

Materials and methods: A single-group, pre-test, and post-test pre-experimental study were conducted. Thirty-one ED patients were prospectively selected according to the eligibility criteria. In each session, 3000 shocks were applied at 5 points over the penis. Eight sessions were delivered in total with a 2–3-day interval. The patient's condition was assessed using the International Index of Electric Function (IIEF-5) questionnaire at baseline and one month after the last treatment session. Paired t-test was used to determine the difference between the pre-test and post-test.

Results: Mean age of the patients was 44.6 (± 14.70) ranging from 25 to 78 years. The majority of them were married (83.9%) and service providers (51.6%). We have also found 51.6% overweight, 9.7% obese, 48.4% diabetic, 45.2% hypertensive, 12.9% with enlarged prostate, 45.2% smoker, 25.8% alcoholic, and 71% with sleep disturbances. During the pre-test, 9.7% had severe ED and 51.6% had moderate ED. After the treatment, no patients were found with severe ED, and few of them had moderate ED (9.7%). The mean difference in IIEF-5 score during the pre-test and post-test was statistically significant (p= < 0.001).

Conclusion: The study showed efficacy of LI-ESWT in a subset of patients with ED. Future studies with larger sample size, placebo group, and longer follow-up periods are recommended.

Keywords: Erectile Dysfunction; Low-Intensity Extracorporeal Shockwave Therapy; Clinical Study; Sexual Disorder

Introduction

Erectile dysfunction (ED) can be described as the persistent inability to attain and maintain the erection of male penis sufficiently during sexual activity resulting in unsatisfactory sexual intercourse (1). This is a very common complaint in men over 40 years of age (2). The prevalence of ED ranges from 2%

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(younger than 40 years) to 86% (80 years or older) worldwide (3). Although ED is a benign illness, it can have a significant impact on patients' physical and psychological well-being, as well as their partners' quality of life (4). ED shares the common risk factors with cardiovascular illness such as lack of exercise, obesity, smoking, hypercholesterolemia, and metabolic syndrome (5). Therefore, ED is considered as a potential indicator of cardiovascular disease and vascular risk factors (VRFs) such as diabetes and hypertension (6,7). Another risk factor of ED is radical prostatectomy (RP) of any type because the treatment procedures carry the risk of cavernosal nerve injury, poor oxygenation of the corpora cavernosa, and vascular insufficiency (8). ED also has different types depending on the etiology, but vasculogenic is the most common type of ED (9).

ED is often underestimated in many developing countries as it is not a life-threatening condition (10) and would resolve on its own (11). Men with ED rarely seek professional advice due to stigma associated with the disease (10). ED an important public health problem and applied research is necessary to meet the increasing demand of clinical services. Since 1998, the application of oral Phosphodiesterase type-5 inhibitor (PDE5i) has gained popularity with 60% recovery rate and patients could lead a satisfactory sex life (12). Intracavernosal injections of vasodilating agents were also given to the patients who do not respond to the oral agents (9). However, those treatment methods have significant limitations (side effects, low response rates) and they are unable to alter the underlying pathophysiology of erectile mechanism (13). For a number of years, low intensity extra corporal shockwave therapy (LI-ESWT) is showing good result in improving male erectile dysfunction (13, 14,15), also proved to be useful in other medical condition, for example, neovascularization in myocardial ischemia (16).

Since the 1980s, various types of shockwaves have been used for a variety of purposes, including high intensity (pressure ¼ of 450 bar) for the therapies of urolithiasis, medium intensity (pressure ¼ of 200 bar) for the therapies of pain, tendonitis, and bursitis, and even more recently (pressure ¼ of 80 bar) for the treatment of ED (14). Ultrasound therapy improves the quality of vascular endothelial growth factor, which aids in angiogenesis (17). Shockwaves also have a positive influence on the proliferation of heart cells, smooth muscle cells, and vascular endothelial precursors (18). Then LI-ESWT was introduced to treat diabetic foot ulcers and chronic cardiac ischemia (16, 19). The idea of applying LI-ESWT for the treatment of ED came out from a study that revealed that the shockwave energy improved ischemia induced myocardial dysfunction when applied to the myocardium of pigs (16). It is hypothesized that the shockwave might increase the blood flow of penis and improve the endothelial function by stimulating angiogenesis in the corpus cavernosum (14). Though the mechanism is not yet completely clear, however, LI-ESWT has been proved to trigger the release of angiogenetic factors through different pathways that leads to neovascularization (14, 20). Considering the above-mentioned evidence, we aimed to determine whether LI-ESWT could benefit people who were suffering from erectile dysfunction.

Materials and methods

This study was a prospective single-group pretest-posttest pre-experimental research to determine the efficacy of radial LI-ESWT (perform with BTL-6000 SWT, manufacture: BTL industries, Ltd.) among patients with symptomatic erectile dysfunction. The study was conducted in a private physiotherapy treatment center in Dhaka city, Bangladesh during the period of January 2020 to June 2020 for 6 months. Ethical permission was obtained from the ethical review committee of the Department of Public Health, North South University, Dhaka, Bangladesh. Thirty-one patients with erectile dysfunction were selected purposively who came to seek treatment for ED at the center were offered to take part in the study. We have explained the purpose of the study to each patient and obtained their verbal consent for their participation. We have also notified them about their right to refusal at any point of the study.

The first step of the study was screening. Patients were screened according to the eligibility criteria (Table 1) during the first visit. Those who were using the PDE5i had to go to a flush-out period of three weeks before starting the treatment. We have also obtained patient’s previous medical history and conducted a physical examination. All patients were committed to refrain from usage of PDE5i and any other therapies for ED during the duration of the treatment session. During the second step, patients went through shockwave therapy sessions. During each session, patients received 3000 shocks, with intensity of 1.5-2 bars, and frequency of 7-12 Hz (depending on how well the patient can tolerate the given treatment).

Table 1: Eligibility criteria

Inclusion criteria	Exclusion criteria
1. Age > 20 years	1. Surgery of radiotherapy of pelvic region
2. IIEF-5 score between 5-21 (severe to mild).	2. Psychiatric or neurological pathology
3. History of ED > 6 months	3. History of spinal cord injury
4. In a stable relationship (> 3 months)	4. Penile anatomical abnormalities
5. Capable of independent communication	5. Pregnant partner
6. Capable of giving verbal consent	6. Under anticoagulants or anti androgen medications
	Severe cardiac or pulmonary disorders
	Unwillingness to participate in the study

Shocks were applied at 5 points over the penis (3 points on the dorsal side of the penis dividing the whole length of the penis into three, and 2 points at the right corpus cavernosum and left corpus cavernosum on the dorsum at the shaft), 600 shocks in each area (3000 shocks in total) in one session. The treatment areas were the same for every session. A patient received 8 sessions in total with 2-3 days gap from one session to another. Each session took approximately 20-25 minutes. All sessions were performed in an outpatient setting without anesthesia.

Data collection tools: We have collected the data using the abridged 5-item version of the International Index of Electric Function (IIEF-5) as a diagnostic tool before starting the treatment procedure on the first day of treatment. The possible scores for the IIEF-5 range from 5 to 25, and ED as classified into five categories based on the scores: severe (5-7), moderate (8-11), mild to moderate (12-16), mild (17-21), and no ED (22-25). All patients were interviewed again after one month of the last session with the same questionnaires. The interview was conducted by a qualified male physiotherapist in a separate place to maintain confidentiality. Increasing of the IIEF-5 score from pretest to posttest was defined as an improvement of ED.

Statistical analysis: After the data collection, we have checked the data for consistency and errors. We have used the SPSS (Statistical Package for Social Science) version 23.0 for data analysis. Demographic characteristics of the patients were presented using frequency measures. Paired t-test was used to compare the pre-test and post-test score. Findings were considered significant when the P value was less than 0.05.

Results

Demographic and clinical characteristics: A total of 31 patients were enrolled in this study based on the eligibility criteria. Their mean (± SD) age was 44.6 (± 14.70) years, ranging from 25 to 78 years. Majority of the participants were married (83.9%). A large proportion of them were service holder (51.6%) or businessman (41.9%). Mean height of the participant was 5.59 (± 0.26) feet and mean weight was 76.54 (± 12.57) kilograms. Their mean BMI score was 26.02 (± 3.89). Eighteen men had one or more cardiovascular risk factors (e.g., hypertension, hypercholesterolemia). Fourteen people were smokers and 8 people were consuming alcohol on a regular basis. Three were found to have obesity based on the BMI scale and 15 of them had type 2 diabetes mellitus. Four people have also reported to have enlarged prostate and three of them had testosterone deficiency. Twenty-two people had sleep disturbances and twenty of them were also suffering from depression. Fourteen of them had reported to have problems in their relationship with the intimate partner. Few of them were exercising regularly (41.9%) (Table 2).

IIEF-5 score: Among the 31 participants in this study during the pre-test, we found that, only 9.7% (n=3) had severe ED (1-7). Majority (51.6%, n=16) of them had moderate ED (8-11) followed by mild-moderate ED (12-16) (25.8%, n=8). During the post-test (after one month of the last treatment session), no participant was found to have severe ED (1-7). Few of them (9.7%, n=3) had moderate ED (8-11), and majority of them (48.4%, n=15) were found to have mild-moderate ED (12-16) (Figure 1).

We have further analyzed the mean difference of IIEF-5 score during the pre-test and post-test using the pared t-test.

The test result indicates a statistically significant difference between IIEF-5 score before treatment (m=11.61, SD=3.61) and IIEF-5 score after one month of the treatment (m=15.90, SD= 3.66); 95% CI (3.51, 5.07), (t (30) = 11.20, p= <0.001). This entails the improvement in ED scores after the treatment sessions.

Table 2: Demographic and clinical characteristics of the patients

Characteristics	Number (%)
Marital Status	
Married	26 (83.9%)
Unmarried	5 (16.1%)
Occupation	
Service holder	16 (51.6%)
Businessman	13 (41.9%)
Retired	2 (6.5%)
BMI (kg/m^2)	
Underweight (<18.5)	1 (3.2%)
Healthy (18.5 - 24.9)	11 (35.5%)
Overweight (25 - 29.9)	16 (51.6%)
Obese (>30)	3 (9.7%)
Diabetes	
Yes	15 (48.4%)
No	16 (51.6%)
Hypertension	
Yes	14 (45.2%)
No	17 (54.8%)
Problems in relationship	
Yes	14 (45.2%)
No	17 (54.8%)
Enlarged prostrate	
Yes	4 (12.9%)
No	27 (87.1%)
Smoker	
Yes	14 (45.2%)
No	17 (54.8%)
Sleep disturbances	
Yes	22 (71.0%)
No	9 (29.0%)
Alcohol consumption	
Yes	8 (25.8%)
No	23 (74.2%)
Exercise habit	
Sometime	13 (41.9%)
Regular	10 (32.3%)
Never	8 (25.8%)

Discussion

The purpose of ED treatment for men should be an attempt to rehabilitate or cure from the illness. The common treatment modalities such as PDEFI or intracavernosal injections of vasodilating agents are non-curative (13). In this study, our endeavor was to supplement evidence to the alternative treatment options for patients with ED. Use of LI-ESWT was started in the medical field in late 1990s and this unique modality of shockwave expanded as a potential treatment option for ED (14). Previously, only one study conducted in Bangladesh regarding the use of LI-ESWT in ED (21), this study made another attempt to verify the clinical application of LI-ESWT in ED patients in a similar population.

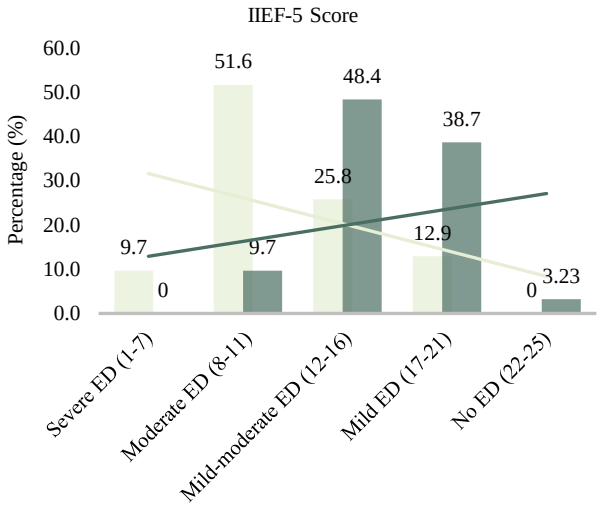

Figure 1: IIEF-5 score during pre-test and post-test

In our study, we have used the radial LI-ESWT twice per week over the period of 4 weeks (8 sessions in total). The assessment was made at the first session before the treatment and after 4 weeks from the last treatment session. Similar arrangements have been applied to other studies; therefore, we can compare our findings in light of those previous studies (13, 21). In our study, we have evaluated 31 patients with ED and found significant improvements after the treatment with LI-ESWT. Many other randomized, double-blinded, placebo-controlled trial proved the efficacy of LI-ESWT in patients with ED (13, 15, 22). The first randomized, double-blinded placebo-control trial reported that the LI-ESWT had a positive short-term clinical and psychological effect in patients with ED who also responded to the PDE5i oral agent treatment. The IIEF-EF score was significantly higher among the treatment group than their counter art (15). However, in a similar setting, Yee et al. did not find any significant evidence in the IIEF score among patients under LI-ESWT treatment compared with the placebo group (13). Similar results were also reported by a recent double-blinded trial. A positive long-term efficiency of linear focused shockwaves was reported in patients with vasculogenic ED (22). Another open-label, single-arm prospective study recruited participants who did not responded to the PDE5i, provided with the same

regime of LI-ESWT. A total of 29 men participated in the study, and at week 13 of the trial, the mean IIEF-ED score increased significantly than the baseline (p= 0.035) (23). A narrative review also reported that the patients (60% to 75%) who responded to PDE5i could obliterate their dependency on those oral drugs and achieve an erection and vaginal penetration when treated with LI-ESWT. They have also reported that 72% who were non-responsive to PDE5i before undertaking LI-ESWT became responders and achieved vaginal penetration (24).

Another open-label prospective study used electromagnetic shockwave unit of higher energy density (previously used to treat patients with tenosynovitis and tendinitis) to treat 30 patients with ED. They assessed the efficacy and safety of the regime and reported that, following 6 weeks of interventions (2 sessions per week), 60% of the patients showed an improved erectile response according to the IIEF-5 scale, the effect remained for 4 months (25). In a multicenter study with higher number of population and 6-month follow-up, showed 81% efficacy in the treatment of ED (26). Another similar study showed 76% efficacy, following a 3- month follow-up in a group of 31 patients (27).

Our study revealed positive responses of radial LI-ESWT when applied to the patient with ED, therefore recommends as a potential treatment modality for such an illness. It is also suggested to be the alternative treatment option to PDEF5i (13). However, the number of patients recruited in this study was comparatively small, and we lack the involvement control group which could give us a concrete conclusion. Further studies with larger sample size and placebo group could provide promising evidence for LI-ESWT. It was also evident from previous animal studies that application of LI-ESWT induces neovascularization and cell-proliferation after 4-weeks (28, 29). The cellular level response following the application of LI-ESWT have corresponded to the positive outcome when patients were assessed after 4-weeks of treatment with LI-ESWT in our study and other similar studies (13, 21). However, the follow-up period after 1-month in this study was relatively short to draw the conclusion regarding the long-lasting benefit of LI-ESWT for ED patients. Further studies with longer follow-up period could give us a better understanding. Furthermore, we could not record any vascular modifications in the penis, future studies could include penile vascular analysis through doppler as a follow-up examination which may indicate changes in cavernosal arteries after LI-ESWT. Observation of physiological and anatomical changes following the application of LI-ESWT would allow us to generate more suitable treatment protocol in administering the doses and intervals, also to define appropriate target group for such treatment. It is also worth mentioning that a patient was considered responsive to LI-ESWT when he showed improvement in the IIEF-5 score, but that does not necessarily confirm a patient's successful sexual intercourse.

Although PDE5i is commonly used treatment option for ED, however, 10-25% of patients have reported side effects such as dyspepsia, flushing, headache etc. (30). In this study, no patient reported any adverse effect of LI-ESWT, therefore we can expect this treatment modality to be safe and effective. Many other studies have endorsed the good safety profile of LI-ESWT (13, 14, 21). With many clinical and observational evidence cited above, this non-pharmacological treatment modality seems promising for the treatment of ED, particularly patients with vascular risk factors (VRFs).

Conclusion

This single-group pre-experimental study showed that radial LI-ESWT improved patient's IIEF-5 score in a subset of population diagnosed with ED with a relatively short follow-up period. We recommend further studies to include larger sample size with a placebo group. Further studies also require to validate optimal targets and ideal protocols to arrive at a conclusion. In the future, this non-pharmacological treatment modality for ED can be widely used in Bangladesh, which is now very rarely used.

Conflict of Interests

Authors declare no conflict of interests.

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