Low-Intensity Extracorporeal Shockwave Therapy versus Oral Therapy in the Management of Mild and Moderate Erectile Dysfunction: A Prospective Randomized Study

Abstract

Background: One developing strategy for the treatment of Erectile Dysfunction (ED) involves the utilization of noninvasive low intensity extracorporeal shockwave (LI-ESWT) therapy. This method shows promise in enhancing erectile function, while also demonstrating satisfactory levels of safety and efficacy. The objective of the present investigation was to assess the safety and effectiveness of LI-ESWT in comparison to phosphodiesterase type 5 inhibitor (PDE5i) treatment for males experiencing mild to moderate ED.

Methods and patients: This prospective randomized controlled trial (RCT) was done on sixty male individuals with ED with mild to moderate ED degree (index of erectile function (IIEF 5) =twelve-sixteen), married with stable heterosexual relationship for more than six months, proved to had vasculogenic ED etiology and vasculogenic ED by doppler,. Patients were randomly categorized into two equal groups by (Block randomization). Group A: underwent LI ESWT and Group B: received sildenafil hundred mg on demand.

Results: There was a important development in Erectile Hardness Score (EHS), IIEF-5, self-esteem and relationship (SEAR) scores at the treatment of the first and third months of in both groups when compared with level of baseline. Indicate that there were no important variance among group A and group B in terms of the IIEF-5, EHS at follow-up and baseline.

Conclusions: The findings of the research indicate that Li-ESWT had comparable efficacy to sildenafil in terms of treatment outcomes, as assessed by IIEF-5, SHE questionnaire. The observed enhancements in the EHS and IIEF-5 measures indicate that both interventions effectively improved function of erectile

Keywords: ED, Low-Intensity Extracorporeal Shockwave Therapy, Oral Therapy

Introduction:

Erectile dysfunction (ED), also referred to as erectile disorder, denotes the condition characterized by the incapacity to achieve and sustain an erection that is deemed sufficient for engaging in sexual intercourse or other related activities. The phrase ED use is more commonly opposed over the term "impotence." In its diagnosis of Erectile dysfunction (ED), the Statistical and Diagnostic Manual of Mental Disorders-5 (DSM-5) stipulates a minimum length of six months. [1].

According to the findings of the Massachusetts Male Aging research. there was a rate of prevalence of fifty-two percent. The research findings indicate a positive correlation among age and the ED prevalence. Specifically, the research indicates that the likelihood of experiencing ED elevates as individuals grow older. by the age of forty, approximately forty percent of men are afflicted by this condition, while by the age of seventy, the prevalence rises to over seventy percent among males. The incidence of total ED exhibited a notable rise, ranging from five percent among individuals aged forty to fifteen percent among those aged seventy. [2].

ED can be categorized into two primary etiologic categories: organic and psychogenic. The organic causes of a condition can be attributed to hormonal, vasculogenic and neurogenic etiologies. The main category of etiologies is vasculogenic, where inflow or arterial abnormalities are the prevailing reason. [3].

The phosphodiesterase type 5 inhibitor (PDE5i) utilization is presently prevalent and represents the most efficacious therapeutic approach for those suffering from ED. Certain patients may exhibit a lack of response to the administered medication due to a variety of factors. In such cases, alternative treatment options are frequently considered, including the penile prosthesis implantation and injection of intracorporal [4].

In the United States, the Food and Drug Administration (FDA) has licensed several oral PDE5i for ED treatment. These include, avanafil. sildenafil, tadalafil, and vardenafil. Several other PDE5i have received regulatory approval for utilization in different cities. [5].

The clinical application and investigation of extracorporeal shock wave therapy (ESWT) have been explored in multiple medical domains, yielding varying levels of success. High-intensity shock wave therapy is employed in lithotripsy due to its concentrated mechanical disruptive characteristics, while medium-intensity shock waves have demonstrated anti-inflammatory attributes and are utilized in the treatment of various orthopedic ailments, including bursitis, non-union fractures, and tendonitis. [6].

In contrast, LI-ESWT is an emerging treatment method that has angiogenetic features. Consequently, it is employed in the control and treatment of peripheral neuropathy persistent wounds, ED and heart neovascularization. [6].

This research aimed to test the hypothesis that LI-ESWT's neovascularization induction would lead to enhanced cavernosal artery flow, hence enhancing erectile function and making LI-ESWT a viable, noninvasive therapy option for ED [6].

The objective of this research was to evaluate the safety and efficacy of LI-ESWT compared PDE5i for men with mild to moderate ED.

Methods:

This prospective RCT was done on sixty adult male individuals more than twenty years with mild to moderate ED degree (IIEF 5 =twelve-sixteen), married with a stable heterosexual relationship for more than six months, and proved to had vasculogenic ED by Penile Duplex Ultrasound (US). The research was carried out from August 2021 to August 2022 after approval from the Ethical Committee at Tanta University Hospitals, Egypt. All patients provided informed written permission.

Exclusion criteria were prior history of pelvic radiotherapy or prostatectomy, cardiovascular previous failed penile implant diseases that prevent sexual activity and neurogenic ED (e.g.: - spinal cord injury, prostatectomy, Parkinson's disease, multiple sclerosis (MS). These individuals were randomly categorized into two equal groups by (Block randomization): Group A: complaining from ED undergo LI ESWT and Group B: complaining from ED take PDE5i in the form of sildenafil hundred mg on demand. All individuals were subjected to: history taking, general clinical examination [consultation with cardiologist and psychiatrist, complete general examination, genital examination, and neurological examination], imaging investigations [Penile Duplex Ultrasound], usual laboratory investigations [Complete blood count (CBC), kidney and liver function test], specific tests [HbA1c, fasting random blood sugar, serum testosterone and serum lipid and prolactin profile].

The IIEF-5 is designed to assess the effectiveness of medical treatments for ED. The survey comprises a total of five inquiries, with each item of IIEF-5 being evaluated on a five-point ordinal scale. In this scale, lower scores indicate a lower level of sexual functioning. ED is categorized into four groups according to the results obtained from the IIEF-5 questionnaire. These categories are defined as follows: severe ED (scores ranging from one to seven), moderate ED (scores ranging from eight to eleven), mild to moderate ED (scores ranging from twelve to sixteen), mild ED (scores ranging from seventeen to twenty-one), and no ED (scores ranging from twenty-two to twenty-five). Patients with an IIEF-5 score ranging from twelve to sixteen are suitable candidates for therapy.

The Confidence Domain and the Relationship Domain make up **SEAR**. It was created to highlight the detrimental impact of ED on mental health and the ameliorative outcomes of effective treatment. Scoring. We added up the responses to each question in order to get domain (Sexual Relationship, between one and eight items; Confidence, 9–14 items); subscale (Self-Esteem, nine to twelve items; Relationship, 13–14 items); and total (items 1–

14) scores. All questions were evaluated from 1 (nearly never/never) to 4 (most times/much more than half of the time), with the exception of questions eight and eleven, which were phrased negatively. **Erection hardness score (EHS):** Tests for ED and the inability to get or keep an erection strong enough for intercourse. Patients with an EHS more than 1 are considered therapeutically suitable. The utilization of this scale facilitates the precise assessment of the severity of ED and its response to therapy, benefiting both you and us.

The score is:

1. The size of the penis is larger than normal, although it lacks rigidity.
2. Rigid, but not solid enough for penetration.
3. Rigid enough for penetration but not completely hard.
4. fully rigid and completely hard.

Participants were randomly assigned to either a nine-week Li-ESWT or an on-demand sildenafil therapy group after a four-week recovery period and thorough explanation. The Li-ESWT protocol is composed of two sessions per week for three weeks. A small device containing a shockwave source (Gymna shock master 300, Germany) is reached with the aid of a specialized probe (silicone pad 10).

The penis was manually stretched, and the shockwaves were sent to the left and right crura, as well as the distal, proximal and intermediate penile shaft. Each LI-ESWT session lasted from fifteen to twenty minutes and consisted of three thousand six hundred shocks delivered at an energy density of 0.09 mJ/mm2 and a rate of 120 per minute.

The sessions were conducted in a cyclical manner with a three-week gap between each repetition. Li-ESWT is administered during each therapy session for a duration of approximately fifteen to twenty minutes. During the trial period, participants in the LiESWT group are prohibited from using sildenafil or any other kind of PDE5i pills. The individuals involved in the administration or consumption of pharmaceutical substances.

The experimental group received on-demand sildenafil therapy at a dosage of hundred milligrams administered one hour prior to each instance of sexual intercourse. The IIEF-5, EHS, and Sexual Encounter Profile (SEP) were evaluated at the first and subsequent three-month periods after the commencement of therapy. The assessment of the side effect profile was conducted at each visit throughout the duration of the treatment period.

Statistical analysis:

The statistical analysis was conducted using SPSS v20 software (Armonk, NY: IBM Corp). The Shapiro-Wilk test was employed to assess the adherence of the distribution to the assumption of normality. The quantitative data were summarized and analyzed using various statistical measures including the range, average, interquartile range (IQR), standard deviation (SD) and median. The chi-square test is a method of statistical commonly employed to assess the differences between numerous categories and analyze categorical data. The Fisher's Exact or Monte Carlo correction method is employed to address the issue of chi-square correction when the predicted count in over twenty percent of the cells is below five. The Student t-test is a statistical test commonly employed to compare two groups in a study, specifically for quantitative variables that follow a normal distribution. The Mann-Whitney test is employed to compare two investigated groups using quantitative variables that are not regularly distributed. The Friedman test is employed to analyze quantitative variables that do not follow a normal distribution. It is utilized to compare multiple periods or stages. For paired comparisons, the Post Hoc Test (Dunn's) is applied. The statistical significance of the acquired results was evaluated using a significance level of five percent.

Results:

There were important variances among the studied groups regarding ED duration. There were no important variances among the studied groups regarding age, risk factors and BMI Table 1

Table 1: Comparison between the two studied groups according to, disease duration (months) , risk factors and demographic data

		Group A (n = thirty)	Group B (n = thirty)	t	p
Age (years)		34.87 ± 2.64	33.67 ± 3.37	1.537	0.130
BMI (kg/m^2)		26.14 ± 2.54	25.95 ± 1.91	0.316	0.753
Duration of disease (months)		23.16 ± 3.05	16.88 ± 2.03	9.380*	<0.001*
Risk factors	**Hypertension(HTN)**	16 (53.3%)	15 (50%)	0.067	0.796
	DM	12 (40%)	12 (40%)	0.000	1.000
	Cardiovascular disease	3 (10%)	4 (13.3%)	0.162	FEp=1.000
	Current smoking	6 (20%)	5 (16.7%)	0.111	0.739

Data are demonstrated as average ± SD or frequency (%). BMI, *: Statistically significant at $p \leq 0.05$.

There were no important variances among the studied groups regarding kidney functions, lipid profile and diabetes profile Table 2

Table 2: Comparison between the two studied groups according to kidney function, diabetes profile and lipid profile

		Group A (n = 30)	Group B (n = 30)	Test	p
Diabetes profile	**HbA1c**	5.93 ± 1.19	5.81 ± 1.58	t=0.323	0.748
	Fasting sugar (mg/dL)	128.2 ± 41.40	134.3 ± 28.90	t=0.665	0.508
Kidney function	**Creatinine (mg/dL)**	0.71 ± 0.11	0.67 ± 0.13	U= 391.0	0.362
	BUN (mg/dL)	14.02 ± 3.98	14.69 ± 4.29	t= 0.627	0.533
Lipid profile	**Cholesterol (mg/dL)**	188.2 ± 22.72	183.1 ± 32.44	0.703	0.485
	Triglycerides (mg/dL)	110.8 ± 46.98	125.5 ± 49.63	1.180	0.243
	HDL (mg/dl)	48.44 ± 12.0	47.24 ± 10.86	0.408	0.684

Data are presented as mean ± SD. HbA1c: Hemoglobin A1C. BUN: blood urea nitrogen. HDL: high-density lipoprotein. p: p value for comparing between the studied periods.

The level of testosterone was higher in group B but without significant difference. While The level of prolactin was higher in group A but without significant difference. All the doppler parameters showed no significant differences between the studied groups. Table 3

Table 3: Comparison between the two studied groups according to testosterone, prolactin and penile doppler

	Group A (n = thirty)	Group B (n = 30)	Test	p
Testosterone (ng/dL)	475.6 ± 166.0	547.6 ± 151.7	1.755	0.084
Prolactin (ng/ ml)	15.78 ± 5.86	14.87 ± 6.63	0.564	0.575

Penile Doppler					
Cause	**Venous**	20 (66.7%)	18 (60%)	χ^2= 0.470	^{MC}p= 0.914
	Arterial	8 (26.7%)	10 (33.3%)		
	Mixed	2 (6.7%)	2 (6.7%)		
PSV		48.50 ± 23.57	45.13 ± 26.49	U= 412.50	0.579
EDV		12.43 ± 8.32	11.33 ± 9.0	U= 402.50	0.482
Resistive index		0.76 ± 0.08	0.78 ± 0.10	t= 0.636	0.527

Data are demonstrated as average ± SD or frequency (%). PSV: Peak systolic velocity, EDV: End diastolic velocity. p: p value for comparing between the studied periods.

There was a high important variance among the three studied periods (before, first month, third month of treatment in both groups regarding EHS, IIEF-5 and SEAR. Table four

Table 4: Comparison between the two studied groups according to EHS, IIEF-5 and EHS, IIEF-5, SEAR and SEAR in each group

		Group A (n = thirty)	**Group B (n = Thirty)**	**U**	**p**
EHS	**Before**	1.77 ± 0.63	1.90 ± 0.66	403.0	0.434
	First month	2.43 ± 0.57	2.70 ± 0.65	351.0	0.100
	Third month	3.10 ± 0.80	3.23 ± 0.63	413.50	0.558
	% of elevate after third month	1.33 ± 1.06	1.33 ± 0.84	444.0	0.926
Fr		31.753*	36.551*		
P		<0.001*	<0.001*		
Sig. bet. periods		p_1=0.033*, p_2<0.001*, p_3=0.007*	p_1=0.001*, p_2<0.001*, p_3=0.033*		
IIEF-5	**Before**	15.80 ± 2.11	15.37 ± 2.37	398.50	0.442
	First month	19.27 ± 1.31	23.57 ± 1.57	22.0*	<0.001*
	Third month	21.77 ± 2.47	21.70 ± 1.64	416.50	0.617
	% of elevate after 3rd month	5.97 ± 3.69	6.33 ± 3.17	418.0	0.635
Fr		45.409*	52.790*		
P		<0.001*	<0.001*		
Sig. bet. periods		p_1<0.001*, p_2<0.001*, p_3=0.017*	p_1<0.001*, p_2<0.001*, p_3=0.007*		
SEAR	**Before**	37.0 ± 5.50	36.37 ± 6.99	449.0	0.988
	1st month	43.53 ± 2.19	51.57 ± 5.46	92.0*	<0.001*
	3rd month	48.57 ± 3.77	46.93 ± 4.46	357.50	0.170
	% of increase after 3rd month	11.57 ± 6.11	10.57 ± 8.85	420.0	0.657
Fr		45.409*	39.200*		
P		<0.001*	<0.001*		
Sig. bet. periods		p_1<0.001*, p_2<0.001*, p_3=0.002*	p_1<0.001*, p_2<0.001*, p_3=0.020*		

Data are presented as mean ± SD. EHS: Erection Hardness Scale. IIEF-5, SEAR: Self- Esteem and Relationship. Fr: Friedman test, Sig. bet. periods were done using Post Hoc Test (Dunn's) p: p value for comparing between the studied periods. p1: p value for comparing between before and 1st month. p2: p value for comparing between before and 3rd month. p3: p value for comparing between first month and third month *: Statistically significant at $p \leq 0.05$.

Discussion

The American Urological Association (AUA) defines ED as the inability to generate and sustain an erection adequate for satisfying sexual intercourse. [7]

The research findings found no important variances among group B and group A in terms of EHS, IIEF-5, and SEAR at follow-up and baseline. However, within group A, there were important developments in, SEAR, IIEF-5, and EHS over the three studied periods. These findings suggest that the treatment received by group A had a positive effect on their sexual satisfaction, erectile function and sexual encounter reliability and ability.

These findings were in convenience with the studies previously done by Lei et al.,[8] as the basal IIEF-5 and EHS were insignificantly different in the studied groups, at the first-month follow-up, the median EHS was significantly higher in the sildenafil group while, median IIEF-5 was significantly higher in the Li-ESWT. However, at the three-month follow-up, there was no important variance in the median IIEF-5 and EHS among the two. SEAR scores were the same between the two groups at baseline. At the first-month follow-up, the SEAR scores were higher in the sildenafil group, but they became equal again at the three-month follow-up.

The shockwaves number used in this research (36000) was higher than in Lei et al.'s [8] study (18000). Overall, both studiessupport the effectiveness of Li-ESWT as an alternative treatment for mild ED in patients who are non-responsive or intolerant to oral therapies.

Egyptian research carried out by Zanaty et al.,[9]. Twenty-six in the Tadalafil group and twenty-five were in the LIESWT group. The SEAR, EHS and IIEF-5 and baseline, six weeks, and twelve weeks follow up EHS were comparable between the studied group.

These findings were in convenience with the researches carried out by Chung et al.,[10].

Baseline, first and third month follow up IIEF-5 were comparable among the studied group. This research is comparable with our research in final finding, that Li-ESWT is effective in

the mild ED treatment. These findings are consistent with the findings of our research, indicating that Li-ESWT is effective in the mild ED treatment. Both studies demonstrate improvements in IIEF-5 scores in the Li-ESWT group compared to baseline values, suggesting the beneficial effects of this treatment modality.

The study by Chung et al. supports our findings that Li-ESWT is an effective treatment option for mild ED. The comparable findings between the two studies further strengthen the evidence for the use of Li-ESWT in improving erectile function.

The research conducted by Caretta et al. [11] demonstrated that at the final of treatment, as well as after three months and six months, the IIEF score of the patients showed important development compared to baseline, the research also reported the average PSV was 40.5 ± 14.4 cm/s, while the average EDV was 2.5 ± 6.1.

The study by Caretta et al. [11] supports our findings that Li-ESWT is an effective treatment option for mild ED, with a majority of patients experiencing a successful outcome and a significant proportion achieving a resumption of normal erectile function. While the use of penile duplex in follow-up, it does not provide specific details about its role in supporting the effectiveness of Li-ESWT. However, penile duplex can be a useful tool in assessing changes in penile blood flow and evaluating the effectiveness of treatments aimed at improving erectile function.

More research with bigger patient samples and penile doppler follow-up is recommended, as is the exploration of therapy scheme adjustments based on parameter improvement. Li-ESWT is another PDE5i alternative for ED patients, particularly those who are unable to take PDE5i and need long-term therapy. It looks to be a successful and safe noninvasive choice for the treatment of ED patients.

Conclusions:

The findings of the research indicate that Li-ESWT had comparable efficacy to sildenafil in terms of treatment outcomes, as assessed by IIEF-5, SHE questionnaire. The observed enhancements in the EHS and IIEF-5 measures indicate that both interventions effectively improved function of erectile.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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