Submitted: 03 May, 2023 Accepted: 12 July, 2023 Published: 30 August, 2023 DOI:10.22514/jomh.2023.076

ORIGINAL RESEARCH

JOMH Journal of Men's Health

A randomized controlled trial of combined low-intensity extracorporeal shockwave therapy and Dapoxetine use in the management of lifelong premature ejaculation

Kazim Dogan[1,*], Mehmet Taskiran[2]

[1]Department of Urology, Faculty of Medicine, Istinye University, 34394 Istanbul, Turkey
[2]Department of Urology, Gaziantep Private Hatem Hospital, 27010 Gaziantep, Turkey

***Correspondence**
kazim.dogan@istinye.edu.tr
(Kazim Dogan)

Abstract

We aimed to evaluate the efficacy of combined low-intensity extracorporeal shockwave therapy (LI-ESWT) and dapoxetine administration for the treatment of lifelong premature ejaculation (LPE) in comparison to LI-ESWT and dapoxetine alone. In the randomized controlled trial, 212 men diagnosed with LPE were enrolled. The participants were randomized into four subgroups: control (n = 50), dapoxetine (n = 56), LI-ESWT (n = 50) and LI-ESWT + dapoxetine (n = 56). The intravaginal ejaculation latency (IELT), premature ejaculation profile (PEP), and Global Impression of Change (GIC) were evaluated. There were substantial improvements in the fold-increase of the IELT (F-IELT), and PEP and GIC-I scores in both the dapoxetine ($p < 0.001$) and LI-ESWT + Dapoxetine ($p < 0.001$) groups than in the control and LI-ESWT groups. Although the LI-ESWT group demonstrated a minor improvement in the F-IELT score ($p = 0.04$), there were no noticeable improvements in the PEP ($p = 0.12$) and GIC-I ($p = 0.15$) scores. In conclusion, a combination of dapoxetine administration and LI-ESWT might be more effective in treating LPE than LI-ESWT or dapoxetine alone, indicating a potential synergistic effect.

Keywords

Premature ejaculation; Therapy; Dapoxetine; LI-ESWT; IELT

1. Introduction

Lifelong premature ejaculation (LPE) is a common sexual dysfunction in men, which is defined as a recurring pattern of ejaculation occurring before or shortly after vaginal penetration, against the individual's wishes [1]. This condition affects males [2] and influences their self-esteem, causing performance anxiety and interpersonal conflicts [3]. The difference between lifelong and acquired PE depends on when the symptoms begin. LPE is characterized by symptoms being present from the first sexual experience. Men with LPE have never experienced a period without PE. The European Association of Urology Guidelines adopted the first evidence-based definition by Society for Sexual Medicine (ISSM), which reflects the complex nature of PE and recognizes it as a medical condition that can severely impact a person's quality of life. Partners of men with LPE frequently encounter decreased sexual desire, lubrication problems and challenges in achieving orgasms, all of which contribute to a decline in their overall sexual life quality [4].

Numerous approaches have been explored to tackle LPE, including medical treatments, behavioral, cognitive-behavioral and pelvic floor therapies, and couple/marriage therapy [5, 6]. Lately, low-intensity extracorporeal shockwave therapy (LI-ESWT) has garnered attention for its potential use in treating erectile dysfunction, chronic prostatitis, and chronic pelvic pain syndrome [7]. Its underlying mechanism is believed to involve the stimulation of angiogenesis and enhancement of cellular regeneration. Applying LI-ESWT to the pelvic floor muscles enhances their strength and control, which could be beneficial in managing LPE. Kalyvianakis *et al.* [8] evaluated the effects of LI-ESWT on erectile dysfunction. Although their study did not explicitly focus on LPE, it did examine the impact of LI-ESWT on sexual dysfunctions. Gruenwald *et al.* [9] demonstrated that LI-ESWT can be an alternative treatment for patients with severe erectile dysfunction, who respond poorly to Fosfodiesteraz 5 (PDE_5)-inhibitor therapy. Manfredi *et al.* [10] reported that LI-ESWT is an established treatment for erectile dysfunction and does not affect the reproductive and hormonal testicular function.

We hypothesize that ESWT increases pelvic floor muscle strength, which improves the motor control over these muscles. This enhanced control, particularly if patients can maintain these muscles in a relaxed state, might delay ejaculation. It might modulate the pelvic neural pathways involved in ejaculation, thereby improving control of the pelvic floor muscles. Additionally, ESWT boosts blood flow, fostering healthier tissues involved in ejaculation. Collectively, these potential mechanisms provide a comprehensive perspective on the possible advantages of using ESWT to manage premature

ejaculation. We aimed to investigate the effectiveness of LI-ESWT and Dapoxetine in treating LPE and determine its potential as a novel therapeutic option. Exploring the combined impact of Dapoxetine and LI-ESWT on LPE will contribute to developing more effective and tailored strategies for the treatment of LPE.

2. Materials and methods

2.1 Study design

A randomized controlled trial was conducted to evaluate the effectiveness of LI-ESWT in treating LPE. We included 212 men who visited the Urology clinic at our hospital, were diagnosed with LPE, and had been administered LI-ESWT. The patients were randomized into four subgroups: "control (n = 50)", "dapoxetine (n = 56)", "LI-ESWT (n = 50)" and "LI-ESWT + Dapoxetine (n = 56)". The participants' demographic character and previous treatment status for LPE were collected using the "Personal Information Form".

2.2 ESWT application

Before initiating treatment, all the patients were provided with detailed information regarding the impact of pelvic floor muscles on premature ejaculation. ESWT was administered to the perineal region once a week, with the aim to produce an effect on the pelvic floor muscles. During each session, 3000 shockwaves were delivered using the Med-Andrology (ME-SWT) device; the probe's location was adjusted after every 600 shockwaves. We followed a rigorous protocol for ESWT application to maximize the effectiveness of the treatment and ensure patient comfort. We utilized a specially designed spacer to optimize the focus of the shockwaves and improve its accuracy. The spacer type was selected based on each patient's unique anatomy to ensuring optimal transmission of shockwaves. Tolerability was a crucial aspect of our protocol. We carefully monitored patients throughout a session for any signs of discomfort or side effects. This protocol was followed consistently across all sessions to ensure uniformity and reproducibility of the interventions.

2.3 Data tools and measurements

The following data collection tools were used in the study: intravaginal ejaculation latency (IELT), expressed as a geometric mean, which was the interval between penetration and ejaculation that was measured using a chronometer [11]; premature ejaculation profile (PEP), where scores <8 indicated premature ejaculation and scores >8 indicated no premature ejaculation [12]; and clinical global impression (GIC-I), which evaluated the clinical improvement after surgical and drug therapy, with scores ranging from zero to seven [13]. We determined the overall change and fold-increase of the IELT (F-IELT) by dividing the geometric mean after treatment by the geometric mean at the beginning of therapy [14].

2.4 Patient grouping

In the dapoxetine and LI-ESWT + dapoxetine groups, 30 mg of dapoxetine was administered. Six sessions of LI-ESWT were administered to the LI-ESWT group at weekly intervals. Each session consisted of administering 3000 pulses to the affected foot with a focused electromagnetic generator (0.25 mJ/mm^2, 8 Hz, 2.5 bars). The location of the probe was changed after every 600 pulses.

2.5 Enrollment

Participants older than 18 years, who were diagnosed according to the Diagnostic and Statistical Manual (DSM)-5 criteria, and consented to participation, were included in the study. Participants had to have LPE without an underlying cause, such as psychiatric illnesses, diabetes mellitus, anatomical abnormalities, urinary tract infections or chronic prostatitis. Additionally, the participants had to have an IELT of <1 min and an LPE Diagnostic Tool score of >11. Furthermore, the participants should have been in a heterosexual relationship for the last six months and not received any treatment for LPE within the same period. The exclusion criteria were as follows: illiterate participants, unwillingness to consent to the interview, patients with medical conditions that could cause LPE (*e.g.*, psychiatric illnesses, chronic prostatitis, abnormalities, urinary tract infections), or those with other sexual dysfunctions in addition to LPE such as erectile dysfunction or low sexual desire.

2.6 Data analysis

All statistical analyses were performed using SPSS Statistics for Windows (Version 22.0. IBM Corp., Armonk, NY, USA) Descriptive data were used to summarize the demographic and clinical characteristics of the study population. The regular distribution suitability of the data was evaluated. Independent samples *t*-test was used to compare continuous variables and chi-square test was used to compare categorical variables between groups. Repeated measures Analysis of Variance (ANOVA) was used to analyze the changes in IELT, PEP and GIC-I scores over time. A p-value of < 0.05 was considered significant.

3. Results

3.1 Demographic analysis

There were no significant differences in age (32.6–34.9 years, $p = 0.549$), waist circumference (86.4–87.1 cm, $p = 0.97$), and complaint duration (11.4–12.2 months, $p = 0.941$) among the four groups. However, there were significant differences in the body mass index (23.4–26.0 kg/m^2, $p = 0.013$), prostate volume (20.5–24.2 cc, $p = 0.001$), glucose levels (87.4 to 99.1 mg/dL, $p = 0.001$), white blood cell count (6.6 to 8.1 $\times$ 10^3/μL, $p = 0.001$), lymphocyte count (1.7–2.7 $\times$ 10^3/μL, $p = 0.001$), neutrophil count (3.7–4.6 $\times$ 10^3/μL, $p = 0.001$), hemoglobin levels (14.8–15.5 g/dL, $p = 0.001$), hematocrit (43.9–44.6%, $p = 0.001$), and platelet count (264.1–338.7 $\times$ 10^3/μL, $p = 0.001$) among the groups (Table 1).

3.2 Paired analysis

In the paired analysis, the four groups were evaluated to understand the effects of different treatments on premature ejac-

TABLE 1. Demographic and laboratory data of all the groups.

Variables	Control	Dapoxetine	LI-ESWT	Dapoxetine + LI-ESWT	*p*-value
Age, yr	32.6 ± 7.4	33.6 ± 8.1	34.9 ± 7.2	33.4 ± 8.4	0.549
Waist circumference, cm	86.4 ± 8.9	87.1 ± 8.3	86.4 ± 7.9	86.6 ± 5.2	0.970
BMI, kg/m^2	23.4 ± 3.4	26.0 ± 3.7	23.4 ± 3.1	25.4 ± 30.0	0.013
Duration of complaint, months	11.4 ± 6.6	11.3 ± 6.5	12.2 ± 8.0	12.1 ± 14.3	0.941
Prostate volume, cc	20.5 ± 4.7	21.9 ± 3.7	24.2 ± 3.7	21.3 ± 3.5	0.001
Glucose, mg/dL	87.4 ± 6.0	97.1 ± 11.7	89.9 ± 5.1	99.1 ± 8.3	0.001
WBC, 10^3/µL	6.6 ± 1.1	7.9 ± 1.9	6.5 ± 1.4	8.1 ± 1.5	0.001
LYMP, 10^3/µL	2.5 ± 0.9	2.5 ± 0.9	1.7 ± 0.8	2.7 ± 0.7	0.001
NEUT, 10^3/µL	4.5 ± 1.0	4.5 ± 1.4	3.7 ± 0.8	4.6 ± 1.5	0.001
HGB, g/dL	15.0 ± 0.9	15.5 ± 1.2	15.0 ± 1.0	14.8 ± 1.1	0.001
HCT, %	45.0 ± 2.7	44.6 ± 2.9	43.9 ± 3.1	44.1 ± 2.9	0.001
PLT, 10^3/µL	304.4 ± 33.1	264.1 ± 87.3	338.7 ± 28.5	267.7 ± 54.2	0.001

BMI: body mass index; WBC: white blood cells; LYMP: lymphocytes. NEUT: neutrophils; HGB: hemoglobin; HCT: hematocrit; PLT: platelets; LI-ESWT: low-intensity extracorporeal shockwave therapy.

ulation. The groups consisted of control, Dapoxetine, ESWT and Dapoxetine + ESWT. Paired sample statistics were used to analyze the data. In the control, there was no alteration in the IELT, PEP and PGIC scores. In the dapoxetine group, there was significant improvement in the IELT (pre-treatment: 27.7 ± 10.6; one month after treatment: 122.5 ± 45; and three months after treatment: 90.5 ± 41; $p < 0.0001$) (Fig. 1) and PEP (pre-treatment: 2.4 ± 1.3; one month after treatment: 9.1 ± 1.7; three months after treatment: 7.6 ± 2; $p < 0.0001$) (Fig. 2) scores. The Patients' Global Impression of Change (PGIC) scale also significantly improved (pre-treatment: 2.96 ± 0.4 and three months after treatment: 3.3 ± 0.6; $p < 0.0001$). In the ESWT group, IELT scores were as follows: pre-treatment, 34.6 ± 14.6; one month after treatment, 36.2 ± 14.7; and three months after treatment, 36 ± 14.1). The PGIC scores remained constant in the ESWT group. In the dapoxetine + ESWT group, the IELT (pre-treatment: 29.1 ± 10.5; one month after treatment: 127.9 ± 45.5; and three months after treatment: 98.2 ± 43.8; $p < 0.0001$) and PEP (pre-treatment: 2.1 ± 1.4; one month after treatment: 9.6 ± 1.9; and three months after treatment: 8.3 ± 2.2; $p < 0.0001$) scores improved. The PGIC also improved in the Dapoxetine + ESWT group (pre-treatment: 2.61 ± 0.6 and three months after treatment: 3.2 ± 0.8; $p < 0.0001$) (Fig. 3).

3.3 Fold increase of IELT

In the F-IELT$_{0-1}$, which is the F-IELT between pre-treatment and the first month of treatment, the dapoxetine group showed a notable increase (5 ± 2.19), as did the Dapoxetine + ESWT group (4.78 ± 1.87). The ESWT group experienced a more modest increase (1.06 ± 0.11) ($p < 0.0001$). In the F-IELT$_{0-3}$ interval, which is the increase between pre-treatment and the third month of treatment, the dapoxetine and Dapoxetine + ESWT groups showed significant F-IELT increases (3.62 ± 1.75 and 3.62 ± 1.68, respectively). At the same time, the ESWT showed a smaller increase (1.06 ± 0.12) ($p < 0.0001$). During the F-IELT$_{1-3}$, the Dapoxetine, ESWT and Dapoxetine + ESWT groups exhibited similar F-IELT increases (0.73 ± 0.14, 1.01 ± 0.09 and 0.75 ± 0.14, respectively) ($p < 0.0001$). Dapoxetine and Dapoxetine + ESWT groups exhibited the most substantial improvements in F-IELT$_{0-1}$ and F-IELT$_{0-3}$ intervals.

4. Discussion

The present study assessed the outcome of LI-ESWT and dapoxetine separately and compared their impact to that of their combined application for the treatment of LPE. Although previous studies have produced conflicting results, our study found a notable increase in the LPE latency time with Depoxetine + LI-ESWT therapy. This combination therapy could be a promising treatment option for LPE, with more favorable outcomes than individual therapy administration. ESWT does not adversely affect the testes or hormones. This finding is indicative of the fact that our study would not demonstrate any negative impacts due to ESWT.

LPE is characterized by symptoms being present from the first sexual experience. Novel approaches for treating LPE include drugs, cognitive-behavioral therapy, or couples' therapy [5, 6]. LI-ESWT has attracted attention for its potential use in treating erectile dysfunction, chronic prostatitis, and chronic pelvic pain syndromes [7, 15]. The underlying mechanism of action of LI-ESWT is believed to involve the stimulation of angiogenesis and enhancement of cellular regeneration. ESWT could modulate the neural pathways in the pelvic region involved in ejaculation and possibly enhance ejaculatory control. This perspective brings to light the role of neural factors in the pathophysiology of premature ejaculation. Enhancing the blood flow to the penile and pelvic regions could promote healthier tissue structures involved in ejaculation. This can significantly impact sexual function given the critical role of vascular health in maintaining normal erectile and ejaculatory functions. ESWT reportedly induces cellular responses that encourage tissue regeneration and improves function. This

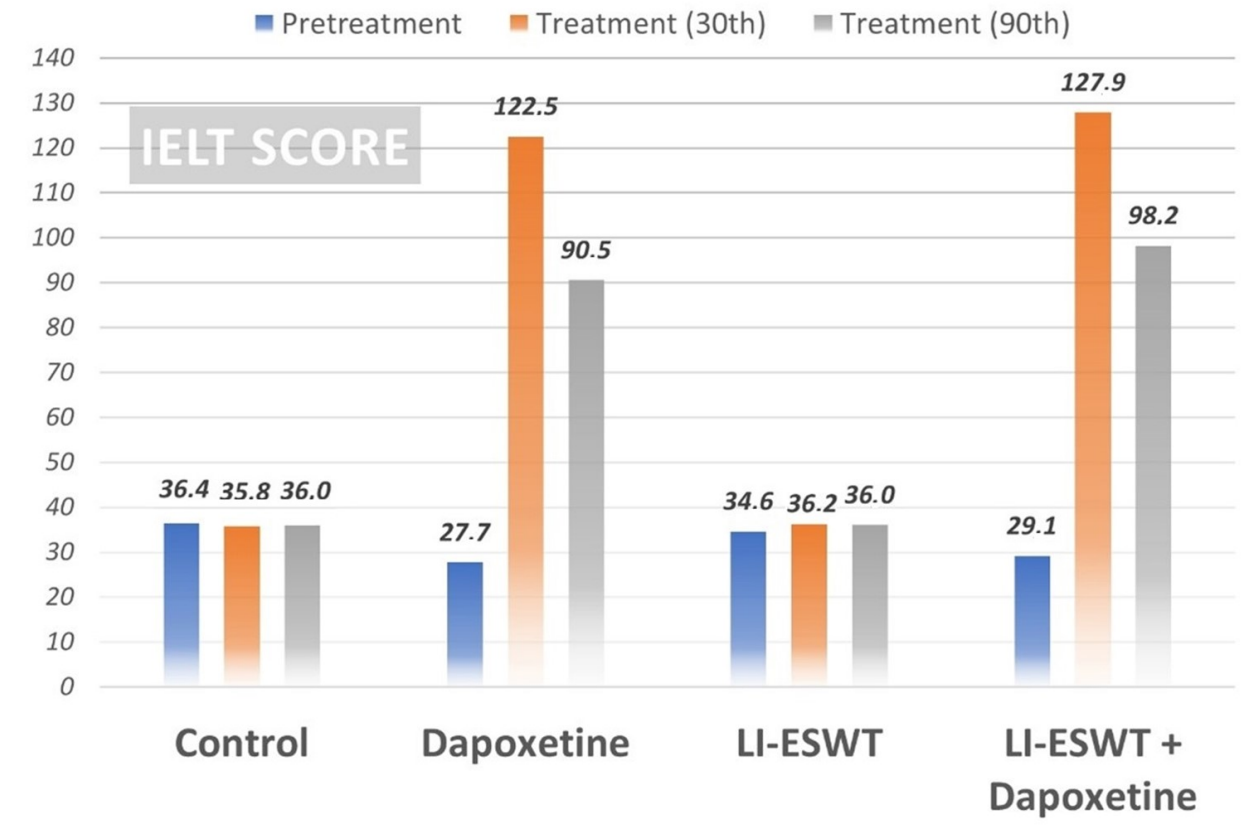

FIGURE 1. Intravaginal ejaculation latency time (IELT) score according to the groups. LI-ESWT: low-intensity extracorporeal shockwave therapy.

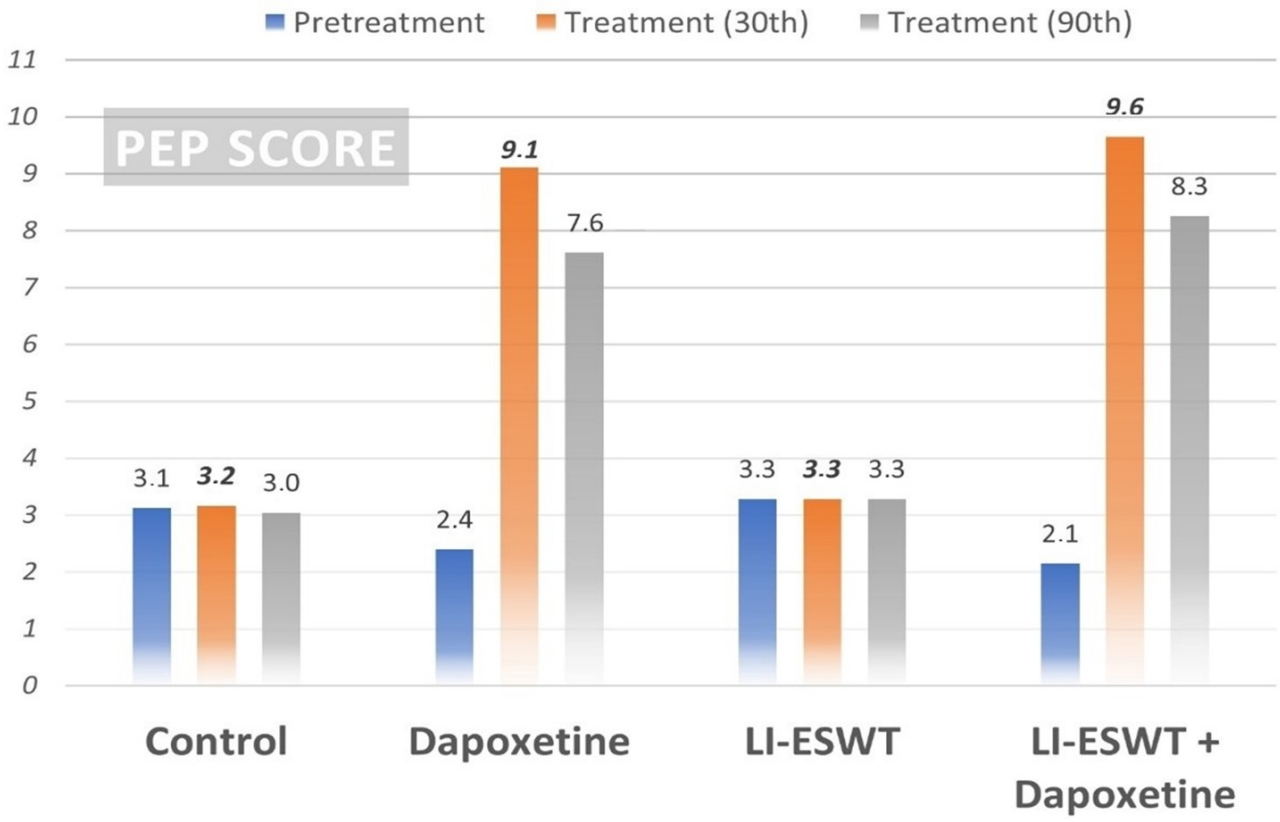

FIGURE 2. Premature ejaculation profile (PEP) score according to the groups. LI-ESWT: low-intensity extracorporeal shockwave therapy.

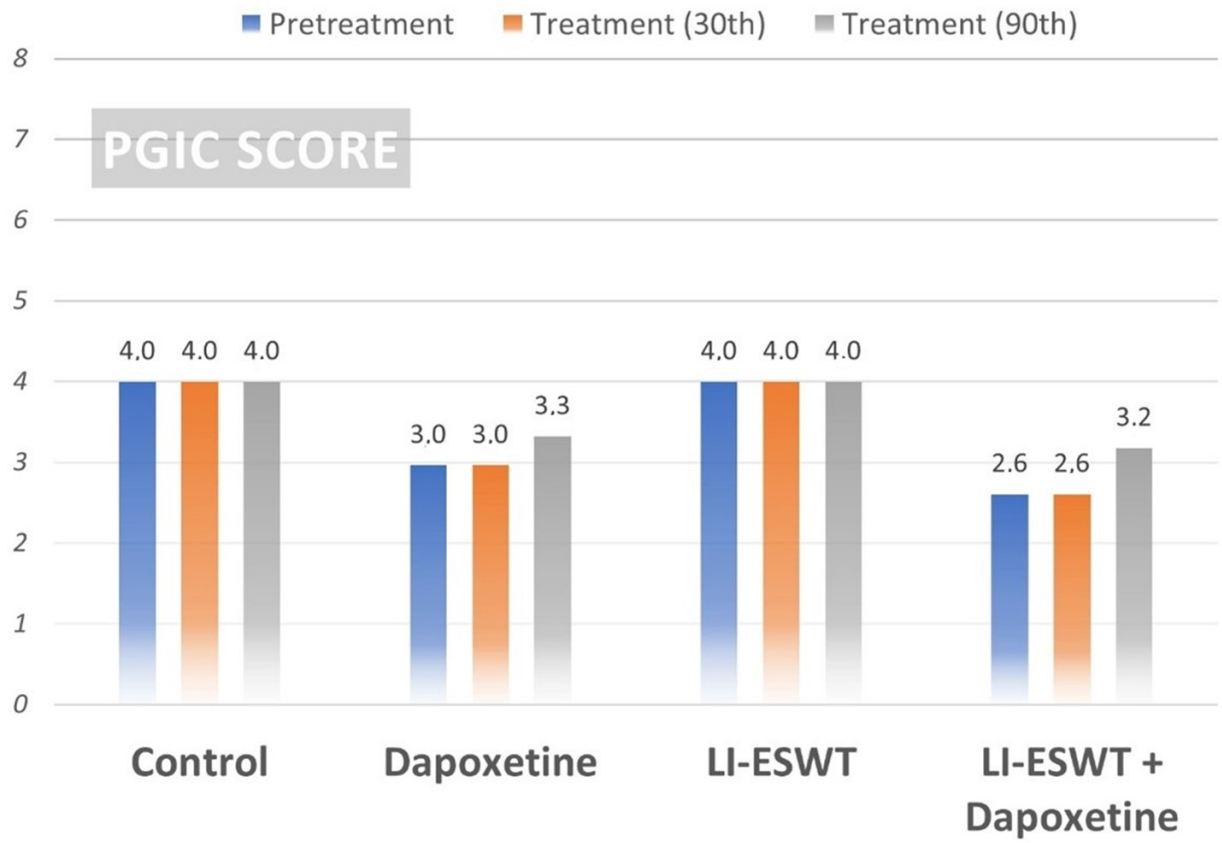

FIGURE 3. Clinical Global Impression (GIC-I) score according to the groups. LI-ESWT: low-intensity extracorporeal shockwave therapy; PGIC: Patients' Global Impression of Change.

could mean improving the function of the structures involved in ejaculation.

Typically, patients with LPE lack understanding about the role of pelvic floor muscles in ejaculation control [16]. Serefoglu *et al*. [17] hypothesized that LPE could be attributed to a selective failure in producing effective contraction of the pelvic floor, rather than early signal reception. Scientific evidence supports the notion that specific muscles and sphincters, such as the ischiocavernosus and bulbocavernosus, play an active role in controlling ejaculation. This was confirmed by a marked increase in electromyographic activity throughout the physiological process [18]. According to Pastore *et al*. [19], physio-kinesiotherapy and electrostimulation can improve the contractile strength of perineal muscles, while biofeedback aids patients in learning to identify and enhance contractions of pelvic floor muscles. This in turn could increase the closing strength of the urethral sphincter. However, for the training of pelvic floor muscles to yield effective results, it usually takes patients several months to comprehend the sequence dynamics, learn to control the ejaculatory reflex, and naturally implement this knowledge during sexual intercourse; the outcomes have been highly satisfactory [20]. Thus, applying LI-ESWT to the pelvic floor muscles could enhance their strength and control and aid in the treatment of LPE [15].

Numerous studies have established that ESWT augments the expression of several neurotrophic factors, such as nerve growth factor and neurotrophin-3, within compromised neural tissue [21, 22]. In a model of bilateral cavernous nerve crush injury, ESWT activated Protein kinase R-like endoplasmic reticulum kinase/Activating Transcription Factor-4 (PERK/ATF4) signaling pathway [23]. Similarly, a previous study established that the expression of neurotrophin significantly increased following an injury in a sciatic nerve injury model treated with ESWT [24]. Furthermore, there is evidence of ESWT inducing the upregulation of nerve growth factor expression following a stroke [25]. Collectively, these findings indicate that ESWT can significantly enhance the expression of multiple neurotrophic factors in damaged neural tissues [26].

Ventus *et al*. [27] compared the effectiveness of cognitive therapy and pharmacology treatment in premature ejaculation. They determined that both treatment modalities effectively improved the IELT. However, cognitive-behavioral therapy had a more lasting effect. Gruenwald *et al*. [9] analyzed the impact of LI-ESWT on penile hemodynamics in patient with LPE. They found that LI-ESWT improved penile blood flow and resulted in an increase in the IELT. Another study which evaluated the impact of LI-ESWT on ejaculation latency [28] determined that LI-ESWT improved the IELT. Furthermore, the study reported improvements in ejaculation latency and overall sexual satisfaction. Our study also showed a minor improvement in the IELT scores but not in the PEP and PGIC scores; this indicated that LI-ESWT did not produce a strong effect alone in the treatment of LPE.

There have been crucial developments in novel drug trials aimed at treating LPE [29]. A randomized controlled trial that compared the effect of dapoxetine to that of a placebo in men with LPE [30] determined that dapoxetine administration

produced a significant improvement in IELT than the placebo did. Althof *et al*. [31] analyzed the efficacy of various pharmacological drugs for LPE. Their results indicated that selective serotonin reuptake inhibitors, including dapoxetine, were influential in prolonging IELT. Our study also observed an increase in IELT as well as the PEP and PGIC scores in the dapoxetine group. LPE was effectively treated in the dapoxetine + ESWT group based on the IELT, PGIC and PEP scores. This indicates that integrating dapoxetine administration with ESWT application effectively improves IELT and PEP, while increasing the overall PGIC.

When interpreting our study results, it is essential to consider several limitations. First, our study included a relatively small sample size due to the participants being randomized into four groups; thus, the results may not represent the broader population of men with LPE. Second, our study results may have limited generalizability to other settings as it was conducted at a single center. Third, followed up duration was short and limited to 90 days. Finally, the study did not include a placebo control group, which may limit the ability to draw firm conclusions about the effectiveness of LI-ESWT compared to other treatments or no treatment at all.

5. Conclusions

Our study findings indicate that ESWT does not adversely affect the testes or hormones. This finding proved that our study would not produce any negative impacts due to ESWT. Treatment with dapoxetine or a combination of dapoxetine and LI-ESWT showed the most significant improvements in the IELT, PEP and PGIC scores. Thus, a combination of dapoxetine and ESWT may be more effective in treating premature ejaculation than ESWT or dapoxetine administration alone. This indicates that dapoxetine and LI-ESWT may have a potential synergistic effect. Further studies with more participants at multiple centers need to be conducted to externally validate our study findings.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

KD and MT—designed the research study; analyzed the data and wrote the manuscript. KD—performed the research. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was conducted in accordance with the Declaration of Helsinki according to the guidelines prescribed by our institutional review board and relevant international standards for research involving human subjects. The study was approved by the Clinical Research Ethics Committee of the Istinye University (Date: February 2023; ID: 23-125). Before proceeding with the treatment, the authors obtained informed consent from the patients, ensuring they were fully aware of the potential risks and benefits involved.

ACKNOWLEDGMENT

Not applicable.

FUNDING

This research received no external funding.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Gurkan L, Oommen M, Hellstrom WJG. Premature ejaculation: current and future treatments. Asian Journal of Andrology. 2008; 10: 102–109.

[2] Laumann EO, Nicolosi A, Glasser DB, Paik A, Gingell C, Moreira E, *et al*. Sexual problems among women and men aged 40–80 y: prevalence and correlates identified in the global study of sexual attitudes and behaviors. International Journal of Impotence Research. 2005; 17: 39–57.

[3] Hobbs K, Symonds T, Abraham L, May K, Morris MF. Sexual dysfunction in partners of men with premature ejaculation. International Journal of Impotence Research. 2008; 20: 512–517.

[4] Althof SE. Psychological approaches to the treatment of rapid ejaculation. The Journal of Men's Health & Gender. 2006; 3: 180–186.

[5] Pastore A, Palleschi G, Fuschi A, Al Salhi Y, Zucchi A, Bozzini G, *et al*. Pelvic muscle floor rehabilitation as a therapeutic option in lifelong premature ejaculation: long-term outcomes. Asian Journal of Andrology. 2018; 20: 572–575.

[6] Ventus D, Jern P. Lifestyle factors and premature ejaculation: are physical exercise, alcohol consumption, and body mass index associated with premature ejaculation and comorbid erectile problems? The Journal of Sexual Medicine. 2016; 13: 1482–1487.

[7] Wu WL, Bamodu OA, Wang YH, Hu SW, Tzou KY, Yeh CT, *et al*. Extracorporeal shockwave therapy (ESWT) alleviates pain, enhances erectile function and improves quality of life in patients with chronic prostatitis/chronic pelvic pain syndrome. Journal of Clinical Medicine. 2021; 10: 3602.

[8] Kalyvianakis D, Hatzichristou D. Low-intensity shockwave therapy improves hemodynamic parameters in patients with vasculogenic erectile dysfunction: a triplex ultrasonography-based sham-controlled trial. The Journal of Sexual Medicine. 2017; 14: 891–897.

[9] Gruenwald I, Appel B, Vardi Y. Low-intensity extracorporeal shock wave therapy—a novel effective treatment for erectile dysfunction in severe ED Patients who respond poorly to PDE5 inhibitor therapy. The Journal of Sexual Medicine. 2012; 9: 259–264.

[10] Manfredi C, Arcaniolo D, Amicuzi U, Spirito L, Napolitano L, Crocerossa F, *et al*. Impact of extracorporeal shockwave therapy for erectile dysfunction and Peyronie's disease on reproductive and hormonal testicular function. Andrology. 2022; 10: 1368–1375.

[11] Waldinger MD, Quinn P, Dilleen M, Mundayat R, Schweitzer DH, Boolell M. A Multinational population survey of intravaginal ejaculation latency time. The Journal of Sexual Medicine. 2005; 2: 492–497.

[12] Burbridge C, Symonds T, Osterloh IH, George K, Lloyd-Price L. Content validity of the premature ejaculation profile, original and per-event formats, in men with lifelong premature ejaculation. The Journal of Sexual Medicine. 2019; 16: 569–576.

[13] Gnanasakthy A, Barrett A, Norcross L, D'Alessio D, Romano CD. Use of patient and investigator global impression scales: a review of food and

drug administration—approved labeling, 2009 to 2019. Value in Health. 2021; 24: 1016–1023.
[14] Waldinger MD, Zwinderman AH, Olivier B, Schweitzer DH. Geometric mean IELT and premature ejaculation: appropriate statistics to avoid overestimation of treatment efficacy. The Journal of Sexual Medicine. 2008; 5: 492–499.
[15] Fode M, Lowenstein L, Reisman Y. Low-intensity extracorporeal shockwave therapy in sexual medicine: a questionnaire-based assessment of knowledge, clinical practice patterns, and attitudes in sexual medicine practitioners. Sexual Medicine. 2017; 5: e94–e98.
[16] Siegel AL. Pelvic floor muscle training in males: practical applications. Urology. 2014; 84: 1–7.
[17] Serefoglu EC, Saitz TR, Trost L, Hellstrom WJG. Premature ejaculation: do we have effective therapy? Translational Andrology & Urology. 2013; 2: 45–53.
[18] Pischedda A, Fusco F, Curreli A, Grimaldi G, Pirozzi Farina F. Pelvic floor and sexual male dysfunction. Urological and Andrological Sciences. 2013; 85: 1–7. (In Italian)
[19] Pastore AL, Palleschi G, Leto A, Pacini L, Iori F, Leonardo C, *et al*. A prospective randomized study to compare pelvic floor rehabilitation and dapoxetine for treatment of lifelong premature ejaculation. International Journal of Andrology. 2012; 35: 528–533.
[20] Pastore AL, Palleschi G, Fuschi A, Maggioni C, Rago R, Zucchi A, *et al*. Pelvic floor muscle rehabilitation for patients with lifelong premature ejaculation: a novel therapeutic approach. Therapeutic Advances in Urology. 2014; 6: 83–88.
[21] Peng D, Tan Y, Reed-Maldonado AB, Lin G, Lue TF. Molecular mechanism of action of low-intensity extracorporeal shockwave therapy for regenerating penile and peripheral nerves. To be published in Turkish Journal of Urology. 2020. [Preprint].
[22] Wang HJ, Su CH, Chen YM, Yu CC, Chuang YC. Molecular effects of low-intensity shock wave therapy on L6 dorsal root ganglion/spinal cord and blood oxygenation level-dependent (BOLD) Functional magnetic resonance imaging (fMRI) Changes in capsaicin-induced prostatitis rat models. International Journal of Molecular Sciences. 2022; 23: 4716.
[23] Wang B, Han Y, Tanaka G. Interplay between epidemic spread and information propagation on metapopulation networks. Journal of Theoretical Biology. 2017; 420: 18–25.
[24] Lee J, Kim S. Effects of Extracorporeal Shock Wave therapy on functional recovery and neurotrophin-3 expression in the spinal cord after crushed sciatic nerve injury in rats. Ultrasound in Medicine & Biology. 2015; 41: 790–796.
[25] Lee J, Sung Y, Jang S. Nerve growth factor expression in stroke induced rats after shock wave. Journal of Physical Therapy Science. 2016; 28: 3451–3453.
[26] Raissi GR, Ghazaei F, Forogh B, Madani SP, Daghaghzadeh A, Ahadi T. The effectiveness of radial extracorporeal shock waves for treatment of carpal tunnel syndrome: a randomized clinical trial. Ultrasound in Medicine & Biology. 2017; 43: 453–460.
[27] Ventus D, Gunst A, Arver S, Dhejne C, Öberg KG, Zamore-Söderström E, *et al*. Vibrator-assisted start–stop exercises improve premature ejaculation symptoms: a randomized controlled trial. Archives of Sexual Behavior. 2020; 49: 1559–1573.
[28] Vardi Y, Appel B, Jacob G, Massarwi O, Gruenwald I. Can low-intensity extracorporeal shockwave therapy improve erectile function? A 6-month follow-up pilot study in patients with organic erectile dysfunction. European Urology. 2010; 58: 243–248.
[29] Althof SE, McMahon CG, Waldinger MD, Serefoglu EC, Shindel AW, Adaikan PG, *et al*. An update of the international society of sexual medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE). Sexual Medicine. 2014; 2: 60–90.
[30] Abu El-Hamd M, Abdelhamed A. Comparison of the clinical efficacy and safety of the on-demand use of paroxetine, dapoxetine, sildenafil and combined dapoxetine with sildenafil in treatment of patients with premature ejaculation: a randomised placebo-controlled clinical trial. Andrologia. 2018; 50: e12829.
[31] Althof SE, McMahon CG, Waldinger MD, Serefoglu EC, Shindel AW, Ganesan Adaikan P, *et al*. An update of the international society of sexual medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE). The Journal of Sexual Medicine. 2014; 11: 1392–1422.

How to cite this article: Kazim Dogan, Mehmet Taskiran. A randomized controlled trial of combined low-intensity extracorporeal shockwave therapy and Dapoxetine use in the management of lifelong premature ejaculation. Journal of Men's Health. 2023; 19(8): 92-98. doi: 10.22514/jomh.2023.076.