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Effects of Low-Intensity Extracorporeal Shockwave Therapy on Erectile Dysfunction: A Systematic Review and Meta-Analysis

Raul I. Clavijo, MD,[1,*] Taylor P. Kohn, MD,[2,*] Jaden R. Kohn, BS,[2] and Ranjith Ramasamy, MD[3]

ABSTRACT

Introduction: Low-intensity extracorporeal shock wave therapy (Li-ESWT) has been proposed as an effective non-invasive treatment option for erectile dysfunction (ED).

Aim: To use systematic review and meta-analysis to assess the efficacy of Li-ESWT by comparing change in erectile function as assessed by the erectile function domain of the International Index of Erectile Function (IIEF-EF) in men undergoing Li-ESWT vs sham therapy for the treatment of ED.

Methods: Systematic search was conducted of MEDLINE, EMBASE, and ClinicalTrials.gov for randomized controlled trials that were published in peer-reviewed journals or presented in abstract form of Li-ESWT used for the treatment of ED from January 2010 through March 2016. Randomized controlled trials were eligible for inclusion if they were published in the peer-reviewed literature and assessed erectile function outcomes using the IIEF-EF score. Estimates were pooled using random-effects meta-analysis.

Main Outcome Measures: Change in IIEF-EF score after treatment with Li-ESWT in patients treated with active treatment vs sham Li-ESWT probes.

Results: Data were extracted from seven trials involving 602 participants. The average age was 60.7 years and the average follow-up was 19.8 weeks. There was a statistically significant improvement in pooled change in IIEF-EF score from baseline to follow-up in men undergoing Li-ESWT vs those undergoing sham therapy (6.40 points; 95% CI = 1.78−11.02; I^2 = 98.7%; $P < .0001$ vs 1.65 points; 95% CI = 0.92−2.39; I^2 = 64.6%; $P < .0001$; between-group difference, $P = .047$). Significant between-group differences were found for total treatment shocks received by patients ($P < .0001$).

Conclusion: In this meta-analysis of seven randomized controlled trials, treatment of ED with Li-ESWT resulted in a significant increase in IIEF-EF scores.

Key Words: Erectile Dysfunction; Shock Waves; Randomized Controlled Trial; Meta-Analysis

INTRODUCTION

Erectile dysfunction (ED) is when a man is unable to achieve or maintain an erection for satisfactory sexual performance. ED is estimated to affect one in every five men and, given the aging male population and increasing prevalence of comorbid conditions, it is likely to become even more prevalent.[1] Phosphodiesterase type 5 inhibitors (PDE5is) are often effective in treating patients with ED and are associated with few side effects; however, a significant proportion of men do not respond to therapy.[2] In men who do not respond to PDE5is or cannot tolerate them because of side effects, options such as medicated urethral suppositories for erection, intracorporal injections, and penile prostheses are available.[3] Although these treatment options can be effective, long-term usage rates are hindered by side effects and potential complications.[4] Furthermore, these treatments attempt to improve erectile function without treating the underlying pathophysiology of ED.[5]

Low-intensity extracorporeal shockwave therapy (Li-ESWT) has been proposed as a treatment option for ED with minimal side effects. Vardi et al[6] first reported on the use of Li-ESWT for ED; their rationale was extrapolated from cardiac literature reporting improvements in neovascularization. Recent studies of a diabetic rat model have recently supported the notion that Li-ESWT indeed might induce structural changes that regenerate penile tissue.[7]

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[1]Department of Urology, University of California, Los Angeles, CA, USA;

[2]Baylor College of Medicine, Houston, TX, USA;

[3]Department of Urology, Miller School of Medicine, University of Miami, Miami, FL, USA

*Equivalent contribution.

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AIMS

Given the availability of several randomized sham-treatment–controlled trials studying the effects of Li-ESWT in the treatment of ED, we performed a meta-analysis to determine whether this novel treatment improves erectile function in men with ED when assessed by the International Index of Erectile Function erectile function domain (IIEF-EF) compared with men undergoing sham therapy.[8–14] In addition, from our review of the literature, we sought to provide formal recommendations for future randomized controlled trials.

METHODS

Search Strategy

Randomized controlled trials published from January 2010 (the year that SWT was first used as a treatment for ED[6]) through March 2016 that reported on using the IIEF-EF sore for men with ED receiving Li-ESWT were identified using electronic searches of MEDLINE, EMBASE, and ClinicalTrials.gov. Additional studies were identified by scanning the reference lists of articles identified, searching relevant conference abstracts, and corresponding with study investigators using the approach recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] A flow diagram for study selection is presented in Figure 1. The computer-based searches combined terms: "[(shockwave) OR (shock wave) AND erectile dysfunction]."

Inclusion Criteria and Trial Selection

Studies were included if they were randomized controlled trials of Li-ESWT for ED that reported on the use of the IIEF-EF, a validated six-question questionnaire that assesses erection frequency, erection firmness, penetration ability, maintenance frequency, maintenance ability, and erection confidence on a scale of 0 to 5.[16] The most comprehensive publication was used when there were several involving the same study population. Abstracts of randomized controlled trials from relevant conferences were included in this analysis in accordance with recommendations of the Cochrane Handbook for Systematic Reviews section 6.2.2.4.[17]

Data Extraction

The following information was extracted independently by two trained investigators using a standardized form: authors and publication year, year of study, publication type, practice setting, duration of follow-up, population, SWT regimen, IIEF-EF (six-question form), participant inclusion and exclusion criteria, sample size, geographic locale in which the study took place, mean or median participant age, and model of Li-ESWT machine. All discrepancies were resolved by discussion and adjudication of a third reviewer. Study investigators from most studies were contacted to obtain further information.

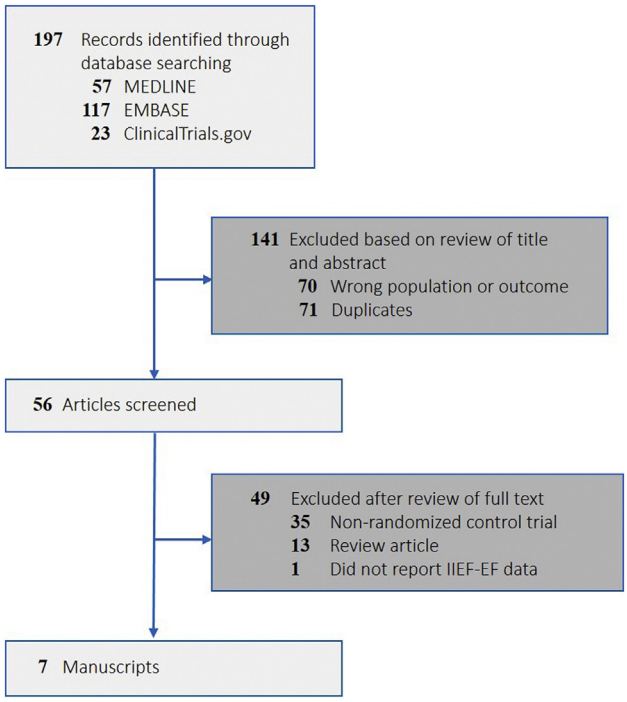

Figure 1. Flow diagram for study selection.

Quality Assessment

The risk of bias in the included randomized trials was assessed using the Cochrane Risk of Bias Assessment tool in the domains of randomization, sequence generation, allocation concealment, blinding, completeness of outcome data, selective outcome reporting, and other potential sources of bias.[17] Domains were independently assessed by two trained investigators (R.I.C. and T.P.K.). All discrepancies were resolved by discussion and adjudication by a third reviewer (R.R.). A graph and a summary for risk of bias were generated with RevMan 5.2.[18]

Data Synthesis and Analysis

The mean differences in IIEF-EF scores measured before initiating and then after treatment with Li-ESWT or placebo were calculated for each study. Overall differences were calculated by pooling the study-specific estimates using random-effects meta-analysis that included between-study heterogeneity.[19] Between-study heterogeneity was assessed by standard χ^2 tests and the I^2 statistic (ie, percentage of variability in prevalence estimates because of heterogeneity rather than sampling error or chance)[20,21] and by comparing results from studies grouped according to prespecified study-level characteristics (total treatment shocks, mean participant age, baseline IIEF-EF score, and duration of follow up) using stratified meta-analysis and meta-regression.[22,23] The influence of individual studies on the overall summary estimates was examined by serially excluding each study in a sensitivity analysis.[24] Bias secondary to small study effects was investigated using the funnel plot and the Egger test.[25,26] All analyses were performed using R 3.2.2 (R Foundation for Statistical Computing).[27] Statistical