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LETTER TO THE EDITOR

Is there a role for extracorporeal shock wave therapy for erectile dysfunction unresponsive to phosphodiesterase type 5 inhibitors?

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Dear Editor

We read with great interest the invited review by Fojecki and colleagues regarding the role of extracorporeal shock wave therapy (ESWT) in urology [1]. The authors systematically reviewed randomized controlled trials (RCTs) published before November 9, 2015, to have examined ESWT in urologic diseases, including Peyronie's disease, chronic pelvic pain and erectile dysfunction (ED). In the article, they focused on the role of ESWT in patients with ED who had previously responded to a phosphodiesterase type 5 inhibitor (PDE5i). Those with ED unresponsive to PDE5is were not mentioned, likely due to lack of RCTs and the assumption that they probably also benefit from ESWT treatment.

The first double-blind, sham-controlled study examining the role of ESWT for PDE5i non-responders was published at the end of 2015 [2] and reported that penile ESWT can convert a PDE5i non-responder to a responder. In terms of erection hardness score (EHS) and the erectile function (EF) domain of the International Index of Erectile Function (IIEF) score, positive outcomes were achieved in 54.1 and 40.5 % of participants 4 weeks, respectively, after completing 12 sessions of ESWT, while no improvement was observed in the sham-controlled group ($p < 0.05$). When the blinded segment of the protocol had been completed, a proportion of patients in the sham control group underwent the same ESWT as those in the treatment group, and their ED also improved significantly. In that study, more than half non-responders were able to achieve an erection hard enough for vaginal penetration (EHS score = 3) with the aid of a PDE5i. Additionally, penile blood flow, measured using the flow-mediated dilation technique, was significantly ameliorated.

In 2012, before the RCT, the same group from Israel had already published their clinical experiences of ESWT in patients poorly responsive to PDE5is, suggesting that it improved non-responders' sensitivity to PDE5is and restored penile hemodynamic response to PDE5is [3]. Despite a lack of consistency in the methods of evaluation used, three other single-arm clinical trials reported promising outcomes of ESWT for PDE5i non-responders [4–6]. According to the current best evidence, the effect of ESWT on this type of ED could last for 4 months [5], and the modality also had the potential to restore spontaneous erection [5]. A summary of the current literature is shown in Table 1.

To illuminate further the potential therapeutic benefits of ESWT on PDE5i non-responders, a large, multicenter, long-term follow-up RCT is still required. Additionally, robust patient selection strategies and the optimal study protocol need to be defined, and the underlying physiological mechanism of ESWT in ED requires exploration.

Nonetheless, in our opinion the current evidence is sufficiently strong to recommend that patients with ED who do not respond adequately to oral PDE5i treatment should be treated with ESWT, before a trial of intracavernous vasoactive drug administration. It appears that ESWT is an effective noninvasive means of improving response to PDE5is and may lead to the recovery of spontaneous EF in some patients.

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Table 1 Summary of current evidence for extracorporeal shock wave therapy in patients with erectile dysfunction poorly responsive to phosphodiesterase type 5 inhibitors

Investigators	Study design	No. of patients	Device	Parameters	Foci (pulses)	Protocol	Concurrent drug administration	Evaluation time	Subjective evaluation	Objective evaluation
Kitrey [2]	RCT	37 (treated) versus 18 (controlled)	Omnispec ED 1000	1500 pulses of 0.09 mJ/mm^2 in a session	Distal, mid and proximal penile shaft, and bilateral crura (300 on each location)	2 sessions/week for 3 weeks, repeated after a 3-week interval	Yes	1 month	Effective rate: 54.1 % (ESWT) versus 0 % (sham) versus 56.3 % (active sham) in EHS; 40.5 % (ESWT) versus 0 % (sham) versus 25 % (active sham) in IIEF-EF; all $p < 0.05$	Significant improvement
Bechara [4]	Single arm	20	Renova NR	5000 pulses of 0.09 mJ/mm^2 in a session	Each corpus cavernosum (900), each crus (1600)	1 session/week for 4 weeks	Yes	3 months	60 % of patients responded to ESWT assessed by IIEF-6, SEP2, SEP3 and GAQ	NA
Chung [5]	Single arm	30	Duolith SD1 ultra	3000 pulses of 0.25 mJ/mm^2 in a session, 6 Hz	Distal penis (1000), base of penis (1000), each crus (500)	2 sessions/week for 6 weeks	No	6 weeks and 4 months	18 (60 %) patients increased ≥5 points in IIEF-5. Of these men, 15 could achieve spontaneous erections enough for penetration. Observed benefits persisted at 4 months	NA

Table 1 continued

Investigators	Study design	No. of patients	Device	Parameters	Foci (pulses)	Protocol	Concurrent drug administration	Evaluation time	Subjective evaluation	Objective evaluation
Ruffo [6]	Single arm	31	Renova	3600 pulses of 0.09 mJ/mm^2 in a session	Each corpus cavernosum and crus (900)	1 session/week for 4 weeks	No	1 and 3 months	(1) IIEF-EF: 16.54 ± 6.35 (baseline) versus 21.13 ± 6.31 (1 month), 21.03 ± 6.38 (3 months). (2) SEP2 (yes): 61 % (baseline) versus 86 % (1 month), 89 % (3 months). (3) SEP3 (yes): 32 % (baseline) versus 58 % (1 month), 62 % (3 months); all $p < 0.05$. (4) GAQ: at 1 month and 3 months, difference was not significant	NA

Table 1 continued

Investigators	Study design	No. of patients	Device	Parameters	Foci (pulses)	Protocol	Concurrent drug administration	Evaluation time	Subjective evaluation	Objective evaluation
Gruenwald [3]	Single arm	29	Omnispec ED 1000	300 pulses of 0.09 mJ/mm^2; overall 1500 pulses in a session	Distal, mid and proximal penile shaft, and bilateral crura (300 on each location)	2 sessions/week for 3 weeks, repeated after a 3-week interval	No use of PDE5i at first follow-up, use at the second	1 and 2 months	(1) Mean IIEF-ED scores increased from 8.8 ± 1.0 (baseline) to 12.3 ± 1.0 at FU1 ($p = 0.035$). At FU2, IIEF-ED increased to 18.8 ± 1.0 ($p < 0.0001$); (2) 72.4 % ($p < 0.0001$) reached an EHS of ≥3 by FU2	Significant improvement at 1 month

RCT randomized controlled trial, *ESWT* extracorporeal shock wave therapy, *EHS* erection hardness score, *IIEF-EF* erectile function (EF) domain of the International Index of Erectile Function, *IIEF-5 and IIEF-6* International Index of Erectile Function questions 5 and 6, *SEP2 and SEP3* Sexual Encounter Profile questions 2 and 3, *GAQ* Global Assessment Question, *NA* not available, *FU1 and FU2* first and second follow-up

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Authors' contribution ZJ Zou and YP Lu wrote and edited the manuscript. ZH Liu and LY Tang collected the data.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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