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Low-intensity shockwave therapy in the management of erectile dysfunction in Singapore

Dear Editor,

Erectile dysfunction (ED) is a distressing condition that affects up to half of men aged 30 and above in Singapore.[1] The prevalence is higher among men with cardiovascular risk factors, and it was reported that up to 63% of uraemic patients had severe ED in Singapore.[2] Low-intensity shockwave therapy (LiST) is a relatively new technology that is indicated for the treatment of ED.[3] The mechanisms involved in LiST include stimulation of mechano-sensors, activation of the neo-angiogenesis processes, recruitment and activation of progenitor cells, improvement in microcirculation, nerve regeneration, remodelling of erectile tissue, and reduction of inflammatory and cellular stress responses.[4] In this study, we prospectively evaluated the outcomes of our patients who received LiST as an adjunct to existing medical therapy for the management of ED.

Recruitment and assessment. The study was approved by the National Healthcare Group Domain Specific Review Board (Reference 2016/01010). Patients who presented to our Urology specialist outpatient clinic for ED were screened. All men above 21 years of age, who selected LiST as one of the modalities for treatment of ED and had a stable relationship with their sexual partner for more than 3 months, were recruited and gave written informed consent. Exclusion criteria included prior treatment with LiST, steroid therapy up to 6 weeks before first treatment, coagulation disorder and testosterone deficiency (total testosterone <8nmol/L). The patients were recruited from April 2017 to December 2017, and followed up from April 2017 to October 2018.

Eligible patients underwent 6 or 12 sessions of LiST. Patients who selected 6 sessions underwent 1 session a week, while patients who selected 12 sessions underwent 2 sessions a week. Shockwaves were delivered using the Duolith SD1 ultra machine (Storz Medical AG, Tägerwilen, Switzerland) in a similar protocol described by Chung and Cartmill.[5] During the treatment period, the patients continued to receive other medical therapies for ED, including phosphodiesterase type 5 inhibitors (PDE5is) and testosterone replacement therapy (TRT) when indicated. The patients' baseline demographics, data on cardiovascular risk factors, testosterone levels, baseline erectile function as determined by the International Index of Erectile Function 5 items (IIEF-5) scores and Erection Hardness Scores (EHS), and Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) scores were recorded. The patients' EDITS was assessed at 1-month follow-up, and IIEF-5 and EHS were assessed at 1-, 3- and 6-month follow-ups. SPSS Statistics software version 22 (IBM Corp, Armonk, US) was used for data analysis. The paired t-test was used to compare the differences in mean values of IIEF-5, EHS and EDITS before treatment and at follow-up visits. The level of statistical significance for all analyses was $P<0.05$.

Results. A total of 19 patients were recruited in the study. The mean age was 57.4 years (range 38–70), and all the patients had a duration of ED of at least 12 months (mean 46.3 months, range 12–120). Fifteen patients (79%) had at least 1 cardiovascular risk factor, which suggested a vasculogenic cause of ED. Six patients (32%) had diabetes mellitus, which suggested a combined vasculogenic and neurogenic cause of ED. All of the patients had been taking PDE5i for at least 3 months; 11 (58%) of whom were taking daily tadalafil, and the other 8 (42%) were taking on-demand PDE5i. Eight patients (42%) were on TRT, and the mean total testosterone of all patients was 13.7±4.0nmol/L at recruitment. Nine patients (47%) had moderate-to-severe ED based on IIEF-5 and EHS ≤2 at baseline, 9 patients (47%) had mild-to-moderate ED, and 1 patient (5%) had a complete response to on-demand sildenafil (IIEF-5=24, no ED).

Fourteen patients (74%) underwent 12 sessions of LiST, while 5 patients (26%) underwent 6 sessions. Sixteen patients (84%) returned for follow-up at 1 month, 17 patients (89%) returned at 3 months, and 11 patients (58%) returned at 6 months. At 1-month follow-up, the mean IIEF-5 for the 16 patients increased from a baseline of 13.1±5.7 to 15.9±6.1 (P=0.002), and the mean EHS increased from 2.44±1.03 to 2.88±0.81 (P=0.014). Three of the 16 patients (19%) had a ≥ 5-point increase in IIEF-5. Of these 16 patients, 15 completed the EDITS score. There was also an improvement in treatment satisfaction, as the EDITS score increased from a mean of 50.1±21.1 to

Table 1. Results outlining mean scores at baseline and follow-ups

	Variable	Mean scores at baseline	Mean scores at follow-up	*P* value
1-month follow-up (n=16)	IIEF-5	13.1±5.7	15.9±6.1	**0.002**[b]
	EHS	2.44±1.03	2.88±0.81	**0.014**[b]
	EDITS[a]	50.1±21.1	67.2±22.3	**0.005**[b]
3-month follow-up (n=17)	IIEF-5	12.7±5.7	17.2±6.5	**0.001**[b]
	EHS	2.41±1.00	2.82±0.95	0.069
6-month follow-up (n=11)	IIEF-5	11.6±6.0	16.9±6.8	**0.001**[b]
	EHS	2.18±1.08	3.00±1.10	**0.02**[b]

EDITS: Erectile Dysfunction Inventory of Treatment Satisfaction; EHS: Erection Hardness Scores;
IIEF-5: International Index of Erectil Function 5 items
[a] 15 of 16 patients completed EDITS
[b] $P<0.05$, significant values in bold

67.2±22.3 (P=0.005). At 3-month follow-up, the mean IIEF-5 for the 17 patients increased from a baseline of 12.7±5.7 to 17.2±6.5 (P=0.001), and the mean EHS increased from 2.41±1.00 to 2.82±0.95 (P=0.069). Eight of the 17 patients (47%) had ≥ 5-point increase in the IIEF-5. These improvements persisted at 6-month follow-up. The mean IIEF-5 for the 11 patients increased by 5.3 points (confidence interval [CI] 95% 2.8–7.9) from 11.6±6.0 to 16.9±6.8 (P=0.001), and mean EHS increased from 2.18±1.08 to 3.00±1.10 (P=0.02), shown in Table 1. Seven of the 11 patients (64%) had a ≥ 5-point increase in IIEF-5 at 6-months. There was no reported adverse event during the study period.

Discussion. In randomised control trials, LiST has been shown to improve IIEF and EHS in treatment groups compared to placebo groups.[6] A meta-analysis which included 14 studies and 833 patients from 2005 to 2015, showed that LiST could significantly improve IIEF (mean difference 2; 95% CI 0.99–3, P<0.001) and EHS (risk difference 0.16; 95% CI 0.04–0.29; P=0.01) with a therapeutic efficacy of at least 3 months.[7] Moreover, LiST had also been shown to convert a PDE5i non-responder to a PDE5i responder.[8]

In our study, we were able to replicate the findings in the early, open label, single-arm, cohort studies[5] with demonstration of statistically significant improvement in mean IIEF-5 at 1, 3 and 6 months, and statistically significant improvement of mean EHS at 1 and 6 months. Furthermore, out of 9 patients who were initially considered non-responders to medical therapy (EHS ≤2), 4 patients responded with EHS ≥3 and a ≥5 -point increase in IIEF-5 at 3-month follow-up. Also, 4 of the 10 patients who were responders to medical therapy had a ≥ 5-point increase in IIEF-5 at 3-month follow-up.

We acknowledge the limitations of our study, such as the lack of a control arm, small number of participants, patient dropout at 6-month follow-up, and the variability in the treatment protocol. In addition, 10 patients (53%) who were considered responders to PDE5i were included in the study.

Nevertheless, our study demonstrated significant improvement in mean IIEF-5 and mean EHS up to 6 months following addition of LiST to conventional medical therapy, regardless of prior response to PDE5i. LiST should be considered a useful adjunct to PDE5i in the management of ED.

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