Long Term Efficacy of Low Intensity Linear Focused Shockwave Therapy for Vascular Erectile Dysfunction Patients: 20 months follow-up

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Objective

Erectile dysfunction is a common medical disorder that primarily affects men older than 40 years of age [1]. Phosphodiesterase type 5 inhibitors (PDE5i) are considered as first-line therapy as they increase arterial blood flow leading to smooth muscle relaxation, vasodilatation and penile erection [2]. The limitation in the efficacy of PDE5 inhibitors is that a 'critical amount' of NO is necessary for these drugs to work. Therefore, in cases of impairment in NO synthesize or release or in cases of destruction of NO, PDE5 inhibitors cannot cure erectile dysfunction (ED) symptoms [3].
Lately, studies have started to evaluate the effect of low intensity shockwave (LISW) to treat ED on PDE5i responders and non-responders patients [4-8].
The current study evaluated how the therapy by a new device ('RENOVA', Initia Ltd, Israel) using low-intensity linear focused shockwave exerts effective and sustainable results at long term follow-up on patients who suffer from ED of vascular origin and experience full, partial or no response at all to PDE5 inhibitors.

Materials and Methods

This study was conducted from March to December 2013. Eligible patients were suffering from Vasculogenic ED for at least 6 months, and their International Index of Erectile Function score (IIEF-EF, [9]) was between 9 and 25 (while on PDE5i). Patients who had hormonal, neurological or psychological pathology or had undergone radical prostatectomy were excluded.
The treatment consisted of 4 weekly sessions. Shockwaves were delivered with a maximum energy of 0.09mJ/mm2; no anesthesia was required. At the end of the full treatment a total of 20000 SW was delivered (6400 shocks at each crura, 3600 shocks at each corpus)
Erectile function was evaluated by means of IIEF-EF, questions 2-3 of the Sexual Encounter Profile (SEP), questions 1-2 of the Global Assessment Questions (GAQ) and the Erection Hardness Score (EHS), at baseline and 1, 3 and 6 months posttreatment. Success was defined as positive answer to both SEP and both GAQ questions, EHS of 3 or higher and an increase of IIEF-EF score from baseline to 6 months follow up according to the severity of the symptoms [10].
Out of 25 patients enrolled to this study, 24 finished the full treatment series.
The mean age was 62.58 ± 8.32 (45-74) years and the mean duration of ED was 4.84 ± 4.46 (1-20) years. 52% were smokers, 26% had diabetes, 58% had high cholesterol levels, 37%

had a cardiovascular disease and 47% had hypertension. 75% of the patients had a positive response to PDE5 inhibitors.
At the end of the treatment and during the follow-up period patients were using PDE5 inhibitors as needed.
14 patients out of 19 patients who had a successfull result in all evaluation parameters at 6 months follow-up were evaluable for long-term follow up (15-21 months; mean 19.8 months). They completed again all the questionnaires.

Results

At 6 months follow-up the overall percentage of patients who achieved positive outcomes at all 4 evaluation questionnaires was 79%.
33% of the PDE5i non-responders (2/6) and 94% of the responders (17/18) achieved positive outcomes at all 4 evaluation questionnaires.
44,4% of the responders stopped using PDE5 inhibitors at 6 month follow-up. None of the patients have reported on pain during or after treatment. No adverse events were reported.
11/14 patients (78.5%) who had a successfull result at 6 months FU, and were evaluable for long-term FU (15-21 months; mean 19.8 months), maintained the advantage gained.
2 patients, PDE5i non responders, continued to respond to PDE5i. Their IIEF at long term FU was respectively 19 (+1) and 23 (-2).
9 patients, PDE5i responders, lost 5 points globally at IIEF-6; SEP and GAQ were unchanged; EHS was reduced from 4 to 3 in only 1 patient and was maintained at 4 in 4 patients.
5 out of these 9 patients had successful intercourses without PDEi or used them occasionally.
3/14 patients (21.4%) did not maintain the advantage gained at the long term FU. IIEF (while on PDE5i), was 20/24/21, 15 points lower (-9/-2/-4) than at 6 months FU; SEP was unchanged (2); EHS was 1 point lower (from 4 to 3) in 1 patient; GAQ dropped from 2 to 0 in all 3 patients.

Discussions

This pilot study was designed for assessing the long term efficacy of a novel device for the treatment of erectile dysfunction, based on an original technology that enables the delivery of low-intensity shockwaves onto a long focal area. The subjects in this study included also patients with multiple co-morbidities, different degrees of response to PDE5 inhibitors and wide range of ED severities. The results of this study demonstrate a possible alternative treatment for some of the patients who did not respond to first-line oral pharmacotherapy and thanks to this treatment may avoid turning to other therapy options which are less convenient to use. In parallel, these data imply on a potential mean to eliminate the need for PDE5 inhibitors which may significantly improve patients' quality of life.
6 months FU showed overall success in 79% of the patients. Success was maintained by 78.5% of these at longer FU (19,8 months mean).
55% of PDE5i responders (at baseline evaluation) continued to have successful intercourses without use of PDEi or using them occasionally.

Conclusion

A growing number of men develops vascular erectile dysfunction because of multiple comorbidities such as diabetes, hypertension, heart disease, dyslipidemia or smoke.
PDE-5 inhibitors, alprostadil injections, vacuum constriction devices and surgical treatment are symptomatic therapies and do not help patients to achieve spontaneous erection. Moreover medications are contraindicated in some conditions and may have side effects. LISWT, is a promising, minimally invasive therapy without side-effects that induce the release of

endothelial nitric oxide synthase, vascular endothelial growth factors and proliferating cell nuclear antigen and thus enhance neovascularization of the penis.
The long-term follow up shows that the vast majority of patients who achieved a positive result from treatment with 20000 low intensity linear shock waves, delivered in 4 weekly sessions, continues to maintain the advantage gained after 19,8 months.
The successful effect of treatment wanes gradually only in 21,4% of the patients.
There is a need for further research to determine if modifications in the treatment protocol (number and intensity) of low-intensity linear focused shockwave could make the positive effect last longer and if an additional treatment could be useful for patients who did not have or lost a successfull result from the treatment.

References

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