High-tone electric muscles stimulation of thigh augments the impaired penile blood flow of diabetic patients without improving symptoms of erectile dysfunction

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Abstract. Objective: Erectile dysfunction (ED) is a major complication in diabetes mellitus. A novel method, high-tone external muscle stimulation (HTEMS), has been proven to be useful in the therapy of diabetic and uremic peripheral polyneuropathy. The aim of this study was to test the potential effect of HTEMS on ED in diabetic patients. Design: An open-label, self-controlled interventional prospective study was conducted at the 2nd Department of Internal Medicine and Nephrological Center, University of Pécs, Hungary. Six Type 2 diabetic patients (mean age 59 ± 7 years) with severe ED (International Index of Erectile Function (IIEF) score: 7.7 ± 8.5) and impaired renal function (eGFR: 61 ± 16 ml/min) were involved. Intervention: The thigh muscles of the patients were treated with HTEMS for 1 h 3 times per week for a duration of 4 weeks. Main outcome measures: Penile peak systolic velocity (PSV) (in the flaccid state and semi-rigid (after 10 mg intracavernous papaverine injection)), IIEF score, quality of life and laboratory parameters. At the beginning also the acute effect of HTEMS on penile PSV was investigated. Results: Under basal conditions penile PSV was rather low. The first HTEMS session of the thighs induced an insignificant increase of PSV in the flaccid state (4.1 ± 1.2 to 6.3 ± 3.3 cm/s) and a significant rise of PSV in the semi-rigid penis (from 6.5 ± 2.5 to 8.9 ± 2.2 cm/s (p = 0.009)). After 4 weeks of HTEMS treatment, under basal conditions no significant change of penile PSV (flaccid and semi-rigid) was observed. Similarly, IIEF score did not improve over the time period (7.7 ± 8.1 vs. 6.7 ± 8.5, p > 0.05). Also, metabolic parameters and eGFR were not influenced. Conclusion: In a pilot study of diabetic patients with severe ED HTEMS of the thighs induced an acute rise of penile PSV in the semi-rigid state. However, after 4 weeks of HTEMS therapy the basal PSV and symptoms of ED were not improved.

Introduction

Erectile dysfunction (ED) is a major problem that affects the quality of life. Its prevalence in the general population is about 5 – 15% and 3 times higher in diabetic patients [2]. The pathogenesis of ED in Type 2 diabetes mellitus is multi-factorial, and includes structural and functional alterations. Accelerated atherosclerosis due to hyperglycemia, hypertension and dyslipidemia leads to a decreased penile arterial blood flow which may be aggravated by renal impairment [3]. Other factors contributing to ED are: endothelial dysfunction and disturbances of the autonomic nervous system.

Lately, in the therapy of diabetic and uremic polyneuropathy the so-called high-tone external muscle stimulation (HTEMS) has been introduced [4, 5]. The device applies a low electrical voltage with a continuously changing amplitude and carrier frequency ranging from 4,096 to 32,768 Hz. The stimulation induces effective muscle contractions as well as increases in blood flow. In diabetic patients HTEMS therapy improved the metabolic control if the treatment was performed daily [6]. Since in the pathogenesis of ED a neuropathic component and a reduced blood flow are involved, the potential effect of HTEMS therapy was investigated.

Patients and methods

The study was approved by the Ethical Board of the University of Pécs. All patients gave their informed consent. Six Type 2 diabetic patients (mean age 59 ± 7 years) with...
severe ED were included. All patients underwent a physical examination by an internist and an urologist, to exclude other causes of ED such as Peyronie’s disease. The baseline investigations included the measurement of penile blood flow, the IIEF questionnaire [7], the visual-analogue scale (VAS), the new neuropathic pain diagnostic questionnaire (DN4 questionnaire) [8] and the hospital anxiety and depression scale (HADS). Among the routine laboratory parameters, hemoglobin A1c, creatinine, fructosamine, total HDL- and LDL-cholesterol and microalbuminuria were analyzed. Prior to the first HTEMS session, PSV of the dorsal penile artery was measured using Hadeco® Bidirectional Doppler ultrasound device. PSV measurement were performed in the unstimulated (flaccid) state as well as after intracavernous injection of 10 mg papaverine (semi-rigid state). The same measurements were performed after the first HTEMS treatment. We used the HiTOP®184 HTEMS device (gbo Medizintechnik AG, Rimbach, Germany) for external stimulation of the thigh muscles. Electrodes were placed on both thighs of the patients. The active electrode on one thigh was connected to the reference electrode of the other thigh and vice versa. Thereby, the electric current was flowing from one leg to the other one.

The HTEMS sessions lasted 1 h each and were performed 3 times a week for 4 weeks. Looking for permanent effects of HTEMS therapy penile blood flow was analyzed both in the flaccid and semi-rigid state after 4 weeks (prior to the last treatment session). Moreover, all parameters were re-investigated. Statistical analysis was performed using SPSS statistical package. After correction for multiple groups, paired-samples t-tests were used for comparison of values prior to interventions vs. values after 1 hour and 1 month of HTEMS therapy. Similarly to that, paired-samples t-tests were used to compare flow measured at the flaccid vs. semi-rigid state.

**Results**

The baseline penile PSV was very low both in the flaccid and semi-rigid state (Figure 1). After the first HTEMS therapy, the PSV in the flaccid state increased insignificantly from 4.1 ± 1.2 cm/s to 6.3 ± 3.3 cm/s and in the semi-rigid state significantly from 6.5 ± 2.5 cm/s to 8.9 ± 2.2 cm/s. At the end of the session (after 60 min of therapy) the acute effect reached a plateau (data not shown). After 4 weeks of therapy, the basal PSV in the flaccid state averaged 3.1 ± 1.5 cm/s and in the semi-rigid state 4.4 ± 0.8 cm/s. This indicated a trend to lower values. Similar to the unchanged penile PSV, the IIEF score did not improve significantly (7.7 ± 8.5 vs. 6.7 ± 8.1). The DN4 score showed a trend to lower values (3.8 ± 2.8 vs. 2.8 ± 2.4) while the HADS score was unchanged (p > 0.05 for all). The blood chemical investigations including hemoglobin A1c did not show any alterations: fructosamine (333 ± 104 vs. 328 ± 116 µM), total cholesterol (4.1 ± 0.7 vs. 4.4 ± 0.6 mmol/l), HDL-cholesterol (0.9 ± 0.3 vs. 0.9 ± 0.3 mmol/l), LDL-cholesterol (2.3 ± 0.6 vs. 2.3 ± 0.3 mmol/l), triglycerides (3.2 ± 1.6 vs. 3.2 ± 1.7 mmol/l) or urinary albumin/creatinine ratio (22 ± 37 vs. 23 ± 44 mg/mmol). The glomerular filtration rate showed a non-significant trend to higher values (eGFR_MDRD: 61.3 ± 16.2 vs. 74.0 ± 16.5 ml/min).

**Discussion**

Erectile dysfunction is an important complication of diabetes mellitus with a complex pathogenetic background: e.g., diabetic polyneuropathy, generalized atherosclerosis and vascular endothelial dysfunction [9]. In a pi-
lot study we analyzed the effect of HTEMS therapy on penile blood flow, ED symptoms, functional and laboratory parameters in a small group of diabetic patients. The patients had a near-target glycemic control (hemoglobin A1c 7.4 ± 1.3%) and showed a severe ED with a very low baseline IIEF score (7.7 ± 8.5). They also had a severe arterial insufficiency as indicated by the very low baseline penile PSV. Values of < 30 cm/s are regarded as a marker of penile arterial impairment [10]. The major finding of our study is that we verify an acute distinct effect of HTEMS therapy on the thighs. We observed a small but significant increase in the penile PSV in the semi-rigid condition despite its severe impairment. However, after 4 weeks of HTEMS therapy, basal penile PSV did not change. There was even a trend to lower values. Similarly, the symptoms of ED did not improve. The rather low DN4 score of 3.8 ± 2.8 showed an insignificant trend to lower values which is in line with previous investigations demonstrating positive effects of HTEMS therapy on diabetic and uremic polyneuropathy [4, 5]. Also the metabolic parameters did not change. It is an open question whether a more frequent HTEMS therapy, for instance in daily intervals, could lead to better results. In fact, Rose et al. showed that daily HTEMS therapy over 6 weeks results in a significant improvement in carbohydrate metabolism [6].

The mechanism behind the HTEMS-induced rise in penile blood flow is unclear. The device uses electric muscle stimulation with a rapidly changing carrier frequency and amplitude to stimulate the muscles. The low frequencies probably induce marked contraction of the muscles whereas the high frequencies may lead to muscle fibration. The muscle stimulation is associated with enhanced blood flow [4]. It is conceivable that the activated striated muscles could release vasoactive substances that might induce distant effects of HTEMS. This assumption is supported by investigations of Peckova et al. [11] who observed an increased diuresis and natriuresis during HTEMS therapy.

**Conclusion**

In a small, open-label, self-controlled intervention study, HTEMS therapy of the thighs in patients with severe ED and vascular dysfunction resulted in an acute improvement in penile blood flow. Within the following 4 weeks of HTEMS treatment (3 times per week), basal penile blood flow and ED were not significantly improved. It is an open question whether a more frequent therapy (daily sessions) in patients with less severe ED might be more successful.

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**Conflict of interest**

The authors of the paper and participants of the study have no conflict of interest to declare.

**References**


