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The effect of high-tone external muscle stimulation on symptoms and electrophysiological parameters of uremic peripheral neuropathy

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Abstract. Objective and design: Peripheral neuropathy is a devastating uremic complication that causes debilitating pain and movement limitation. The aim of the study was to assess the influence of high-tone external muscle stimulation (HTEMS) therapy on clinical and electrophysiologycal parameters in hemodialysis patients with uremic peripheral neuropathy. Patients and interventions: The study group consisted of 28 chronic hemodialysis patients (mean age 71.6 ± 8.6 y, median 74 y) on maintenance dialysis for 3 – 187 months (median 31 months). Eight persons (28.9%) were diabetics. All of them exhibited overt peripheral neuropathy and had undergone pharmacological therapy without improvement. All subjects were treated with HTEMS for 1 h during a hemodialysis session, 3 times weekly for 12 weeks. The dialysis parameters (duration of the session, blood and dialysate flow) were constant during the treatment period. Electrophysiological evaluation before and after intervention included assessment of sensory nerves (ulnar nerve, sural nerve) and motor nerves (ulnar nerve, peroneal nerve). The examined nerve conduction parameters were conduction velocity, amplitude, distal latency and F-wave latency. Results: In the questionnaire 18 persons (64%) reported improvement of general well-being after HTEMS therapy, 17 persons (61%) felt an increase of physical capacity, and 16 persons (57%) experienced a decreased feeling of cold feet. The electrophysiological findings were obtained in 19 patients who completed the examination before and after the course of HTEMS. A significant improvement was noted in the motor conduction velocity of the ulnar nerve; respective values were 48.53 ± 6.14 vs. 51.50 ± 5.51 m/s, p = 0.03. Conclusion: The study demonstrated for the first time that the subjective amelioration of uremic peripheral neuropathy by HTEMS treatment is associated with significant improvement in an objective electrophysiological parameter, motor conduction velocity of the ulnar nerve.

Introduction

Uremic peripheral neuropathy is one of the most frequent complications of end-stage renal disease (ESRD) during the dialysis period [1]. It occurs in ~ 60 – 100% of these patients [2]. Uremic peripheral neuropathy is a distal, symmetrical, mixed sensorimotor neuropathy, with greater lower-limb than upper-limb involvement. The problem has continued to grow in the last decade due to the increasing number of diabetic patients in dialysis programs whose neuropathy may have more complex pathogenesis encompassing a diabetic and uremic background. In some of these patients the symptoms of peripheral neuropathy become a principal element of suffering, constituting a source of devastating pain and limiting the ability to move [3]. There is no effective pharmacological treatment of uremic neuropathy. Intensification of the dialysis regimen, and application of tricyclic antidepressants or anticonvulsants for pain relief, are recommended. However, these measures do not improve the course of neuropathy in the majority of patients. There is a strong clinical need for the implementation of new, more effective therapeutic methods.

Therefore, the aim of the present study was to evaluate the effectiveness of non-pharmacological therapy by high-tone external muscle stimulation (HTEMS) in a group of chronic hemodialysis patients, more than a quarter of them were diabetics.

Material and methods

The study group consisted of 28 chronic hemodialysis patients (mean age 71.6 ± 8.6 y,

Table 1. Results of electrophysiological examination.

Before HTEMS therapy																	
Ulnar nerve (motor)					Peroneal nerve (motor)					Ulnar nerve (sensory)				Sural nerve (sensory)			
	DL	AMP	CV	Flat		DL	AMP	CV	Flat		DL	S-AMP	CV		DL	S-AMP	CV
Mean	3.29	7.74	**48.53***	31.67	Mean	4.54	2.18	34.02	56.36	Mean	3.03	10.32	40.92	Mean	0.63	1.96	10.23
SD	0.58	2.39	6.14	3.60	SD	1.84	2.14	14.42	6.17	SD	1.17	7.94	15.58	SD	1.29	4.28	21.03
Median	3.2	7.4	48.9	31	Median	4.6	1.9	36.8	57.35	Median	3.25	8.2	45.4	Median	0	0	0
Min	2.6	3	34.2	26.9	Min	0	0	0	47.9	Min	0	0	0	Min	0	0	0
Max	4.8	11.5	57.8	39.2	Max	7.8	6.9	62.5	70	Max	5	30	61.7	Max	3.4	14	54.5
After HTEMS therapy																	
Ulnar nerve (motor)					Peroneal nerve (motor)					Ulnar nerve (sensory)				Sural nerve (sensory)			
	DL	AMP	CV	Flat		DL	AMP	CV	Flat		DL	S-AMP	CV	DL	S-AMP	CV	
Mean	3.37	7.35	**51.47***	32.42	Mean	5.30	1.82	37.04	60.23	Mean	2.86	10.47	36.01	Mean	1.12	2.75	14.19
SD	0.50	1.93	5.55	3.20	SD	0.78	2.15	5.40	12.68	SD	1.30	7.21	18.94	SD	1.76	4.76	22.43
Median	3.4	7.3	54.5	32.6	Median	5.1	1.1	36.2	56.85	Median	3.15	10.2	42.8	Median	0	0	0
Min	2.6	4.73	39.6	27.5	Min	4.3	0.1	28	50.8	Min	0	0	0	Min	0	0	0
Max	4.5	12.1	59	38.3	Max	7.3	8.3	50	101	Max	4.2	30	56	Max	4.2	14.6	57.2

DL = distal latency (ms); AMP = amplitude (mV); CV = conduction velocity (m/s); F-lat = F wave latency (ms); S-AMP = SNAPs amplitude (microV). *p = 0.03.

median 74 y) on maintenance dialysis for 3 – 187 months (median 31 months). Eight persons (28.9%) were diabetics. All of them exhibited overt peripheral neuropathy and had undergone pharmacological therapy without improvement. The severity of neuropathy was scored based on a clinical examination performed by two neurologists (M.B., M.K.) who also carried out the electrophysiological measurements. The neurophysiological tests were performed using a Viking Quest Nicolet Biomedical Device. Nerve conduction velocity tests (motor with F-wave estimation and sensory) were conducted in the ulnar, peroneal and sural nerves using standard methods [4, 5]. Motor nerve conduction studies were performed in ulnar and peroneal nerves on the left. Briefly, recording surface electrodes were placed over the abductor digiti minimi muscle or extensor digitorum brevis muscle (for ulnar and peroneal nerves, respectively). A supramaximal stimulus was applied at the distal and proximal points of stimulation. The distal latency, amplitude of the negative component of the compound muscle action potential (CMAP) at the distal point, and conduction velocity between two points of stimulation were assessed. The F-wave of the shortest latency from 20 responses was chosen.

Antidromic sensory nerve conduction studies were performed in ulnar and sural nerves on the left. In the ulnar nerve a stimulating electrode was placed at the wrist over the nerve trunk, while recording ring electrodes were positioned over the little finger. In the sural nerve the sensory nerve action potential (SNAP) was recorded with a surface electrode just behind the lateral malleolus, while a stimulating electrode was placed slightly lateral to the midline on the posterior aspect of the calf at the junction of the middle and lower thirds of the leg. Latency to the first negative deflection of the SNAP and peak-to-peak amplitude were determined.

All subjects were treated with HTEMS for 1 h during a hemodialysis session, 3 times weekly for 12 weeks. The dialysis parameters (duration of the session, blood and dialysate flow) were constant during the treatment period. The procedure was performed using a HiTop 181-H instrument (gbo, Medizintechnik, Rimbach, Germany). The electrodes were placed on the femoral muscles. Amplitude and electrical frequency were modulated simultaneously (initial frequency 4,096 Hz, maximal 32,768 Hz). For each patient, the intensity of the electrical stimulation was adjusted to a pleasant level that did not produce any pain or uncomfortable paresthesias.

After the end of the treatment period all patients completed the questionnaire rating the treatment effects, and 19 patients completed the repeated electrophysiological evaluation. The form contained three questions. The first concerned general well-being, the second physical capability, and the third feeling of cold feet. For each question there were three options for the answer: a) improvement, b) without change, c) deterioration. The patients themselves indicated the appropriate response.

Written informed consent was obtained from all the participants. The study was approved by the Ethics Committee of the Wroclaw Medical University and followed the Declaration of Helsinki.

The data were analyzed by paired Student's t-test (two-tailed); $p < 0.05$ was considered significant (for statistical analysis we used R, ver. 2.12.1, R-Project).

Results

All included patients finished the treatment course. No adverse effects were observed.

In the questionnaire 18 persons (64%) reported a general improvement of well-being after HTEMS therapy, 17 persons (61%) felt an increase of physical capacity, and 16 persons (57%) experienced a decreased feeling of cold feet.

The electrophysiological findings obtained in 19 patients who completed the examination before and after the course of HTEMS therapy are presented in Table 1.

A significant improvement was noted in the motor conduction velocity of the ulnar nerve; respective values were 48.53 ± 6.14 vs. 51.50 ± 5.51 m/s, $p = 0.03$.

Discussion

In the context of the lack of effective pharmacological treatment of peripheral uremic neuropathy, HTEMS may be appraised as a promising tool. Our results confirm the conclusion from a previous study concerning patients' subjective feeling of amelioration of peripheral neuropathy symptoms after HTEMS therapy [6]. In the questionnaire of self-evaluation of HTEMS course effects, 18 persons (64%) reported a general improvement of well-being after HTEMS therapy, 17 persons (61%) felt an increase of physical capacity and 16 persons (57%) experienced a decreased feeling of cold feet. It is worth emphasizing that we revealed for the first time that subjective improvement of the patients after the HTEMS course is accompanied by a positive effect on the objective electrophysiological parameters, with a significant increase of the motor conduction ulnar nerve velocity (respective values 48.53 ± 6.14 vs. 51.50 ± 5.51 m/s, $p = 0.03$) probably via a central mechanism. The ulnar nerve consists of myelinated nerve fibers. Conduction velocity in this type of nerve fiber depends largely on the condition of the myelin sheath. Another electrophysiological parameter, amplitude, is related to the number of fibers in the nerve. In our study, an improvement of conduction velocity was achieved without affecting the amplitude. This may suggest that HTEMS exerts a beneficial effect on the regeneration of myelin sheaths. The results of the electrophysiological examination performed in our study confirm the known fact that uremic peripheral neuropathy is more advanced in the lower extremities.

The electrophysiological abnormalities in the lower extremities were not affected significantly by HTEMS. This may be interpreted as reflecting the irreversibility of the destructive process in sural and peroneal nerves of the legs. It could also be considered as an argument for earlier implementation of HTEMS, even before dialysis treatment, in CKD patients with overt symptoms of peripheral neuropathy, especially in diabetics. Another method of electric therapy, transcutaneous electrical nerve stimulation (TENS), is proposed for consideration in the treatment of diabetics by the American Academy of Neurology [7]. There are no published data on the effect of TENS in uremic patients. In one head-to-head study HTEMS exhibited superiority over TENS in diabetics [8]. Collectively, the current and former studies are strongly in favor of wider application of HTEMS in both the diabetic and uremic population. Randomized trials are strongly warranted to objectively determine the role of HTEMS in the treatment of peripheral neuropathy.

Conclusion

The study demonstrated for the first time that subjective amelioration of uremic peripheral neuropathy by HTEMS treatment is associated with significant improvement in an objective electrophysiological parameter, motor conduction velocity of the ulnar nerve.

Conflict of interest

M.K. and B.S. declare no conflict of interest.

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