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The effects of combined physical procedures on the functional status of patients with diabetic polyneuropathy

Uticaj kombinovanih fizikalnih procedura na funkcionalni status bolesnika sa dijabetesnom polineuropatijom

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Abstract

Background/Aim. Diabetic polyneuropathy is a common chronic complication in patients with diabetes mellitus. The aim of this study was to determine the importance of applied physical procedures on the functional status of diabetic polyneuropathy patients compared to the group of respondents treated by alpha-lipoic acid. **Methods.** Sixty subjects were divided into two groups: group A – diabetic polyneuropathy patients treated with physical procedures, and group B – diabetic polyneuropathy patients treated with alpha-lipoic acid. The study has lasted for three diagnostic and therapeutic cycles, each lasting for 16 days with a time between cycles of 6 weeks. **Results.** Manual muscle test, range of motion, Michigan Neuropathy Screening Instrument, and Berg balance scale values showed statistically significant improvement at the end of testing group A respondents, while no improvement was shown in group B respondents. **Conclusion.** The application of the combined physical procedures shows clear benefits for the improvement of muscle strength and mobility of the ankle joint in respondents with diabetic polyneuropathy.

Key words:
ankle joint; diabetic neuropathies; muscle strength; physical therapy modalities; range of motion, articular; thiotic acid.

Apstrakt

Uvod/Cilj. Dijabetesna polineuropatija (DP) je česta hronična komplikacija kod bolesnika sa dijabetesom melitusom. Cilj rada bio je da se utvrdi značaj primenjenih fizikalnih procedura na funkcionalni status bolesnika sa DP u poređenju sa grupom ispitanika lečenih alfa-lipoičnom kiselinom. **Metode.** Ukupno 60 ispitanika je bilo podeljeno u dve grupe: grupa A – bolesnici sa DP lečeni fizikalnim procedurama i grupa B – bolesnici sa DP lečeni alfa-lipoičnom kiselinom. Studija je bila sprovedena tokom tri dijagnostička i terapijska ciklusa, od kojih je svaki trajao 16 dana, sa periodom između ciklusa od 6 nedelja. **Rezultati.** Vrednosti Manuelnog mišićnog testa, obima pokreta, *Michigan Neuropathi Screening Instrument*-a i Bergove skale ravnoteže pokazali su statistički značajno poboljšanje na kraju testiranja kod ispitanika grupe A, dok kod ispitanika grupe B nije ustanovljeno poboljšanje. **Zaključak.** Primena kombinovane fizikalne terapije pozitivno utiče na poboljšanje mišićne snage i pokretljivosti skočnog zgloba kod bolesnika sa DP.

Ključne reči:
skočni zglob; dijabetesne neuropatije; mišići, snaga; fizikalna terapija, metodi; pokretljivost; tioktinska kiselina.

Introduction

The common chronic complication in patients with diabetes mellitus (DM) is diabetic polyneuropathy (DPN) or distal sensorimotor polyneuropathy (DSP) (in more than 50%, it occurs after 25 years of the disease duration) [1]. There are approximately 600,000 people in Serbia suffering from DM, or 8.2% of the population (out of which 95%

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account for patients with type 2 DM), and 5.9% have diabetic neuropathy [2]. There is an increased risk of deformity, ulceration, and amputation in these patients [3].

DSP leads to postural balance disorders and increased susceptibility to falls [4]. Deterioration of motor nerve fibers weakens the intensity of stimulation of the muscles, which become hypotrophic. Injuries related to falls in these patients are 15 times more often compared to healthy respondents of the same age [5]. In addition, muscle weakness and limitations of mobility in the ankles and the small joints of the foot occur over time. These disorders result in functional foot impairment, changing pressure points on the foot, and the creation of ulceration [6]. Even 30% of diabetics have limited movements of small or large joints. Limited mobility in the ankle joint and metatarsophalangeal (MTPH) joint is caused by the thickening and shortening of the ligaments and tendons, leading to increased plantar pressure of the forefoot [7]. Muscle weakness mainly dominates in the distal segments of the lower limb, thus threatening gait and other activities in daily life [8, 9].

This study aimed to determine the importance of applied physical procedures on muscle strength and range of motion (ROM) in patients with DPN compared to those treated by alpha-lipoic acid (control group of patients). It also aimed to determine whether there was a statistically significant difference in the values of the Michigan test for examining the neuropathy at the beginning and at the end of the study between the group of respondents who underwent the combined physical therapy and the group of respondents who took alpha-lipoic acid.

Methods

This prospective study included 60 randomized patients older than 18 years at the Center for Physical Medicine and Rehabilitation, University Clinical Center Kragujevac, Serbia and was approved by the local Ethics Committee of the University Clinical Center Kragujevac (no. 01-13598 from 22/12/2011). This study was part of the previously published studies by Grbović et al. [10, 11].

Inclusion criteria were the following: DPN with a timeframe longer than 2 months with DPN signs and symptoms defined as pain, muscular weakness, paresthesia, hyperesthesia to anesthesia, and electromyoneurographic (EMNG) findings; without changes in antidiabetic treatment for at least 6 months; patients who signed consent for participation in the study.

Patients who had the following exclusion criteria were excluded from the study: vitamin B12 deficiency, moderate/severe use of alcohol, chronic kidney disease, dysfunction of the thyroid gland, any state of immunodeficiency, diseases of systemic connective tissues, severe damage of the liver, any kind of cerebrovascular ischemia, decompensation of heart failure, presence of acute coronary syndrome in the previous 6 months, uncontrolled high blood pressure (defined as values of systolic blood pressure higher than 160 mmHg and diastolic blood pressure higher than 80 mmHg), chemotherapy in the last decade, severe polytrauma or state after it, use of peripheral nerves damaging drugs (*eg*, nitrofurantoin, paclitaxel, vincristine, cisplatin, indomethacin, emetine, streptomycin, dapsone, chloroquine, ethionamide, isoniazid, carbamazepine, phenytoin, hydralazine, metronidazole, amiodarone); any sort of contraindication for using any of the arranged physical therapy agents (acute infectious disease, fever, pregnancy, malignancy, any acute vital organ failure, the presence of metal in body); or hypersensitivity to galactose, alpha-lipoic acid, Lapp lactose deficiency, or glucose-galactose malabsorption.

The investigation was organized during 3 cycles of diagnostics and therapeutics, each lasting for 16 days with a timeframe between cycles of 6 ± 1 week (total study duration of six months).

All subjects were divided into two groups, 30 patients in each group, with DM type 2 and DSP, in light of clinical indications and signs, just as the parameters of EMNG discoveries. Utilizing computer randomization, every patient was arbitrarily assigned to one group (therapeutical arms): group A or B.

The group A was treated with combined physical procedures that included a pulsed electromagnetic field, exercise, stable galvanization, and transcutaneous electrical nerve stimulation, while the group B was treated with alpha-lipoic acid as per conditions specified in the marketing license in Serbia. Detailed methods applied in these groups can be found in our previously published study [10].

On admission and after completion of the last diagnostical-therapeutical cycle (after 6 months), the EMNG of the lower extremities, Michigan Neuropathy Screening Instrument (MNSI), evaluation of functionality (manual muscle test – MMT and of range of motion – ROM), and Berg balance scale were done. EMNG examination was made with a Medtronic Keypoint device (Denmark, Skovlunde, www.medtronic.com). MNSI comprises two parts. The first part was a questionnaire that consisted of 15 questions, and the second part included the examination of the patient as follows: inspection of the foot (to determine if there are any changes on the feet, ulcerations, infections, calluses, deformities, etc.), the examination of muscle-tendon reflexes, vibratory sensibility testing and examination of monofilaments. The score ranged from 0 (best result) to 10 (worst result), and the score was the result of marks for both legs. Diagnosis of diabetic peripheral neuropathy with a physical examination score higher than 2.5 was established [12]. The examined were *musculus (m.) triceps surae*, *m. peroneus longus*, *m. tibialis posterior*, *m. tibialis anterior* and *m. peroneus brevis*, based on factors of manual loading and gravity. Gradation of muscle strength was performed according to Kendall, namely: 10 points = grade 5 on MMT; 9 = 4+; 8 = 4; 7 = 4-; 6 = 3+; 5 = 3; 4 = 3-; 3 = 2+; 2 = 2; 1 = 2-; 0 = 0, whereby grade 5 matches the strength of a normal muscle which can make a full ROM against gravity and a maximum of manual loading; grade 0 means that during the attempt of a movement, a muscle does not show any visible or palpation sensitive contraction [13].

ROM was tested by dorsal flexion, plantar flexion, eversion, and inversion of the foot. ROMs were measured by a manual goniometer. Active dorsal flexion is normally up to 30°, plantar flexion to 45°, inversion to 35°, and eversion up to 10° [14].

Berg balance scale (BBS) examined the balance in elderly people with vestibular disorders, assessing it through specific functional tasks. This is a valid instrument used to evaluate the efficiency of treatment, the quantitative description of the function in the clinical practice, as well as the research. The scale includes 14 functional tasks for assessing the balance in adults in clinical conditions with grades from 0 (the worst result) to 4 (the best result). The full value of 41–56 indicates a low level of the risk of falling; 21–40 = medium level of the risk of falling; 0–20 = high level of the risk of falling. An eight-point difference is enough to show a change in function between the two measurements [15].

The distribution of all continuous variables was determined using the Shapiro-Wilk test, the median value, minimum and maximum values, and standard deviation (SD). Paired *t*-test was used for comparing the mean values of continuous variables within the tested groups with normal distribution or Wilcoxon's test of matched pairs. Independent *t*-test or the Mann-Whitney test for datasets without a normal distribution were used to compare differences between the groups. For comparison of the frequency (incidence) of categorical (dichotomous) variables, the χ^2 test was used. The *p* values less than 0.05 were considered statistically significant. SPSS version 20.0 was used for statistical calculations. The statistics procedures were the same as in our previously published study [10, 11].

Results

The baseline characteristics of respondents in the groups A and B are given in Table 1. Since this study is part of previously published studies by Grbović et al. [10, 11], the detailed baseline characteristics of respondents from the group A and the group B are given in those manuscripts.

MNSI showed statistically significant improvement at the end of testing the group A respondents ($p < 0.001$), while in the group B respondents, no improvement was shown ($p = 0.169$). BBS examination showed that there was a statistically significant improvement at the end of testing the group A respondents ($p = 0.001$), while in the group B there was no significant improvement shown ($p \approx 1.000$).

At the end of the treatment, there was a significant improvement in the dorsal flexion ($p < 0.001$) and plantar flexion ($p = 0.022$) in the group A respondents. At the start of the study, no significant differences were observed in the measures in the range of motion (homogeneous in dorsal flexion, $p = 0.884$; plantar flexion $p = 0.557$; inversion and eversion of the foot $p \approx 1.000$). At the end of the intervention, both the A and B group respondents did not differ significantly in the observed measures in the range of motion (they were homogeneous in dorsal flexion, $p = 0.055$; plantar flexion, $p \approx 1.000$; inversion of the foot, $p = 0.634$ and eversion of the foot, $p \approx 1.000$) (Table 2).

Table 1

Baseline characteristics of the patients with diabetic polyneuropathy (DPN)

Characteristic	Group A (n = 30)	Group B (n = 30)	*p*-value
Sex, n (%)			
male	11 (36.67)	13 (43.33)	0.598^a
female	19 (63.33)	17 (56.67)	
Heredity for DM, n (%)			
yes	13 (43.33)	13 (43.33)	$\approx 1.000^a$
no	17 (56.67)	17 (56.67)	
Age (years), mean ± SD	63.17 ± 7.68	62.77 ± 8.35	0.09^c
Duration of diabetes (years), mean ± SD	12.22 ± 7.58	11.70 ± 5.75	0.09^c
HbA1c (%), mean ± SD	7.80 ± 1.87	7.30 ± 1.21	0.403^c
MNSI questionnaire, mean ± SD	8.57 ± 1.23	7.83 ± 0.79	0.008^{c*}
MNSI examination, mean ± SD			
before	6.32 ± 0.23	5.95 ± 0.21	0.008^{c*}
after	5.82 ± 0.23	5.87 ± 0.20	0.245^c
p-value	$< 0.001^{b*}$	0.169^b	
Berg balance scale, mean ± SD			
before	43.23 ± 1.28	43.60 ± 1.13	0.244^c
after	43.87 ± 1.28	44.67 ± 1.56	0.34^c
p-value	0.001^{b*}	$\approx 1.000^b$	

DM – diabetes mellitus; HbA1c – glycosylated hemoglobin; MNSI – Michigan Neuropathy Screening Instrument; SD – standard deviation.

Statistical test used: ^{a} – χ^2 test; ^{b} – Paired sample *t*-test; ^{c} – Independent sample *t*-test; * significance at *p*-value < 0.05.

Table 2

Range of motion in the ankle joint

Parameter	Group A (n = 30)	Group B (n = 30)	*p*-value
Ankle dorsal flexion			
before	16.33 ± 4.90	16.17 ± 3.87	0.884[b]
after	19.50 ± 1.52	18.50 ± 2.33	0.055[b]
p-value	< 0.001[a]	0.659[a]	
Ankle plantar flexion			
before	40.50 ± 9.50	41.83 ± 7.93	0.557[b]
after	42.17 ± 6.39	42.17 ± 7.39	≈ 1.000[b]
p-value	0.022[a]	≈ 1.000[a]	
Foot inversion			
before	22.67 ± 6.40	22.67 ± 6.12	≈ 1.000[b]
after	23.33 ± 3.56	22.83 ± 4.49	0.634[b]
p-value	0.058[a]	0.083[a]	
Foot eversion			
before	4.33 ± 1.73	4.33 ± 1.73	≈ 1.000[b]
after	4.67 ± 1.27	4.67 ± 1.27	≈ 1.000[b]
p-value	≈ 1.000[a]	≈ 1.000[a]	

All values are given as mean ± standard deviation. The statistical test used: [a] – Paired sample *t*-test; [b] – Independent sample *t*-test.

Table 3 shows the analyzed muscles of the lower extremities. After the intervention, the A group respondents showed significant improvement in muscle strength of *m. tibialis anterior* ($p = 0.002$), *m. tibialis posterior* ($p < 0.001$), *m. triceps surae* ($p = 0.004$), and *m. peronei* ($p < 0.001$). At the beginning of the study, the A and B group respondents were not significantly different in the followed parameters (homogeneous in muscle strength of *m. tibialis anterior*, $p = 0.55$; *m. tibialis posterior*, $p = 0.32$; and *m. triceps surae*, $p = 0.915$), except in muscle strength of *m. peronei* ($p = 0.024$). At the end of the intervention, the A and B group respondents did not differ significantly in muscle strength of observed muscles (*m. tibialis anterior*, $p = 0.276$; *m. tibialis posterior*, $p = 0.457$; *m. triceps surae*, $p = 0.58$; *m. peronei*, $p = 0.098$).

Discussion

Our study shows the clear benefits of the combined application of physical procedures for the improvement of muscle strength and mobility of the ankle joint in respondents with DPN.

The 2014 study indicated the importance of the implementation of exercise in patients with diabetic neuropathy. The testing included 55 respondents with DPN, 26 of which had exercised (2× per week, 12 weeks), while 29 respondents were in the control group. After 12 and 24 weeks, it led to an improvement in foot functionalities in the intervention group [16].

After a 10-week exercise program, Kluding et al. [17] showed a statistically significant improvement in neuropathic symptoms measured by MNSI ($p = 0.01$), while there was no

Table 3

Manual muscle test values of muscles of the lower extremities

Muscle	Group A (n = 30)	Group B (n = 30)	*p*-value
M. triceps surae			
before	4.47 ± 1.14	4.47 ± 0.97	0.276[b]
after	5.00 ± 1.29	5.03 ± 1.13	0.915[b]
p-value	0.004[a]	0.742[a]	
M. tibialis posterior			
before	4.60 ± 0.97	4.80 ± 1.09	0.457[b]
after	5.03 ± 1.00	5.03 ± 1.29	0.32[b]
p-value	0.001[a]	0.321[a]	
M. tibialis anterior			
before	5.20 ± 1.32	5.40 ± 1.43	0.58[b]
after	5.40 ± 1.38	5.63 ± 1.61	0.55[b]
p-value	0.002[a]	0.096[a]	
M. peroneus longus et brevis			
before	5.00 ± 1.39	4.47 ± 1.04	0.098[b]
after	5.73 ± 1.64	4.83 ± 1.34	0.024[b]
p-value	< 0.001[a]	0.419[a]	

All values are given as mean ± standard deviation. The statistical test used: [a] – Paired sample *t*-test; [b] – Independent sample *t*-test; *M.* – *musculus*.

improvement made in electroneurographic parameters of *n. peroneus*, *n. tibialis* and *n. suralis*. This study was completed by 17 respondents with DPN (8 males/9 females; age 58.4 ± 5.98 years; DM duration of 12.4 ± 12.2 years) or 63.3% of respondents who started the program, which correlates with the results obtained in our study. However, our study also showed improvement not only in the manual muscle test but also in some electroneurographic parameters [10], which could be a result of the combined effect of different physical procedures rather than just exercises used in the study by Kluding et al. [17]. Bosi et al. [18] conducted a study on the effect of pulsed electromagnetic fields in the treatment of diabetic neuropathy, which included 101 respondents (the first group consisting of 50 respondents with the applied pulse magnetic field and the second group consisting of 51 respondents who received placebo). MNSI was being examined and, at the end of the study (3 months later), showed no significant differences between the two groups. Since this study used only the pulse magnetic field and we used multiple physical procedures, again, we could only hypothesize that the improvement in MNSI score in our study was the result of the combined physical procedures.

The 2007 study [19] examined the effect of alpha-lipoic acid in diabetic neuropathy. It included 95 respondents with DPN. The first group included 52 respondents who had been receiving alpha-lipoic acid (600 mg, parenterally) for 14 days, and the second group included 43 respondents with placebo treatment applied. MNSI was examined 7 and 14 days later. There were statistically significant reduced values of the Michigan questionnaire for testing neuropathy in a group of respondents with the applied alpha-lipoic acid ($p < 0.01$) [19]. In our study, we found that multiple physical procedures had a significant effect on MNSI score, but not for patients treated with alpha-lipoic acid. However, patients treated with alpha-lipoic acid had significantly lower MNSI scores before starting the treatment than patients treated with physical procedures.

The study by Song et al. [20] indicated the importance of applying exercise to improve the balance in patients with DPN. After the 8-week exercise implementation (60 min, 2× per week), a statistically significant improvement in balance was made (BBS, $p < 0.05$). As in this study, our study showed that in patients treated with physical procedures, a statistically significant improvement was made in postural equipoise and balance measured by BBS ($p = 0.001$). The group B respondents showed no statistically significant improvements.

Another study indicated the weakness of the foot muscles and limited mobility of the foot joints and ankle joints in patients with DPN, which later became risk factors for foot deformities and ulceration [21]. At the end of our study, the clear effects of the combined application of physical procedures were shown in increasing the range of motion in ankles (dorsal and plantar flexion), while in the second group, such an effect was not achieved.

The study by Andersen et al. [9] also dealt with the examination of muscle strength in patients with DM. The study involved two respondent groups, 36 respondents each (the first group consisted of those suffering from DM, and the second control group consisted of healthy respondents). Muscle strength was determined by using an isokinetic dynamometer. At the end of the study, it was concluded that the first group of respondents had the decreased muscle strength of flexor and extensor of the knee, ankle, wrist, and elbow joint and that it is associated with neuropathy [9]. The importance of the exercise applied in patients with DPN was confirmed in the study by Francia et al. [22]. The study included 26 patients with DM and 17 patients in the control group. After 12 weeks of an exercise program, there has been an increase in muscle strength, mobility, and walking speed, thus preventing the occurrence of disabilities [22].

Similarly to the results of these studies, in our study, at the end of the treatment, we found a significant increase in muscle strength of tested muscles (*m. tibialis anterior*, *m. tibialis posterior*, *m. triceps surae*, and *m. peronei*), while in the group B respondents with the alpha-lipoic acid treatmen, no improvement was made.

Conclusion

The application of the combined physical procedures (pulsed electromagnetic field, exercise, stable galvanization, and transcutaneous electrical nerve stimulation) shows their clear benefit for the improvement of muscle strength and mobility of the ankle joint in respondents with DPN. This is reflected in a significant improvement of neurological symptoms and signs (MNSI), as well as in strengthening muscles and increasing mobility of the respondents, and in improving postural balance.

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Conflict of interest

The authors declare no conflicts of interest.

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