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Research Article

Aerobic Training Improves Symptoms of Neuropathy and Quality of Life in Patients with Diabetic Peripheral Neuropathy

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Abstract

Background: Painful symptoms of diabetic peripheral neuropathy (DPN) is common in patients with type 2 diabetes mellitus (T2DM), which can reduce the quality of life. The effect of aerobic training on neuropathic symptoms and quality of life in people with type 2 diabetes with peripheral neuropathy was investigated in the present study.

Methods: Twenty-four patients with DPN participated in this randomized controlled study. Participants were randomly assigned to the experimental or control groups. The experimental group underwent exercise training consisting of 20-45 minutes aerobic training on the treadmill at 50%-70% of heart rate reserve over three months. Before and after the experimental period, blood samples were taken in a fasting state, and Michigan Diabetic Neuropathy Score (MDNS), monofilament test and quality of life (QOL), and sleep quality (SQ) questionnaires were completed. Data analysis was performed using repeated-measures ANOVA.

Results: In the experimental group MDNS score significantly improved compared with the control condition ($P<0.05$). There was a significant difference between groups regarding 10 g monofilament test score ($P<0.05$). Moreover, QOL and SQ significantly improved in the experimental group with a significant inter-group difference ($P<0.05$). Hemoglobin A1c (HbA1c) level decreased by 7.4% in the experimental group, which was statistically different from the control group ($P<0.05$). Pearson's correlation indicated a significant correlation between HbA1c level and monofilament score.

Conclusion: Regular aerobic training over a short period potentially improves symptoms of DPN and QOL. Lowered levels of HbA1c were correlated with improved foot sensation.

Keywords: Type 2 diabetes mellitus, Diabetic neuropathy, Exercise training, Pain, Life quality

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Background

Type 2 diabetes mellitus (T2DM) is a metabolic disorder with increasing incidence, especially in developing countries (1). T2DM is related to several complications, such as peripheral neuropathy. It is a chronic complication of diabetes characterized by demineralization and degeneration of axons in peripheral nerves (2). Neural damage in diabetic peripheral neuropathy (DPN) can result in several symptoms in this population, including hypersensitivity and loss of pain (2). Chronic symptoms of DPN can lead to signs of depression, anxiety, and mental and physical dysfunction and consequently reduce the quality of life (QOL) (3, 4). It has been reported that DPN leads to depression, disrupts sleep, and reduces the QOL, especially in patients with painful DPN (5). Following this, pain-relief strategies such as pharmacological interventions are prescribed to mitigate pain and probably improve the QOL in this population (6). This is the main intervention for this population, but it is just a pain-relief strategy that may not be an effective prevention/treatment method (7). Since the main mechanisms in the etiology of DPN are suggested to be metabolic and vascular abnormalities, any intervention to set them as a target would eventually prevent the progression of disease (8).

Exercise training is a recommended and effective way to control glycemia and hyperglycemia-related complications in diabetes (9). Exercise training has been established to lower insulin resistance and hemoglobin A1c (HbA1c), and improve the metabolic profile and vascular function in T2DM. In a meta-analysis, Umpierre and colleagues suggested that physical activity was associated with glucose control and lower HbA1c in patients with T2DM (10). Moreover, Nyberg et al suggested that regular physical activity potentially increases vasodilators and diminishes vasoconstrictors, and consequently improves vascular function (11). One study showed that exercise and electrical stimulation increased axonal regeneration following peripheral nerve injury (12). Exercise training also leads to neural improvements, which may be clinically important to patients with DPN. Kluding and colleagues reported that exercise training increased intraepidermal

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nerve fiber branching and reduced pain in DPN (13). In addition to these physiological effects of exercise training, it also increases the QOL in people with T2DM (14). Patients with T2DM with DPN experience more severe symptoms than those without DPN (15). Thus, the QOL consequences of exercise training in these people may be different with patients with T2DM without DPN and depends on its impact on neuropathic symptoms. Any intervention to reduce pain may have a direct impact on aspects of life QOL in this population.

Objectives

Therefore, we aimed to investigate the effect of regular aerobic training on symptoms of neuropathy, QOL, and sleep in patients with DPN and its relation with HbA1c.

Methods

Participants and Design

This was a randomized-controlled parallel-design study. Thirty-one patients volunteered to participate in the present study based on the inclusion criteria. Inclusion criteria were; having T2DM for more than five years, HbA1c > 6.6%, DPN diagnosis, and an inactive lifestyle. The presence of DPN was confirmed by a neurologist based on initial assessments using the Michigan Diabetic Neuropathy Instrument (scores > 3) and abnormal electrophysiological measures at lower limbs. Patients with foot ulcers and orthopedic issues were not included in this study. The participants were not engaged in any exercise program and had no experience of regular exercise participation. A complete description of the aims and procedure of the research was given to the subjects, and then they signed the written consent form.

Participants were randomly allocated to the experimental and control groups, and 12 individuals completed the trial in each group. The experimental group was familiarized with the exercise protocol over a week prior to the main experimental period. During this period, the participants performed 15-20 m walking on the treadmill with the least range of intensity to be familiarized with the exercise procedure. Then, they performed the main aerobic exercise program over 3 months. Exercise training consisted of walking or running at 50%-70% of heart rate reserve lasting 20-45 min each session with a frequency of three sessions/week. Karvonen equation was used to assess target heart rate, and heart rate was monitored using a polar heart rate monitor (PE3000, Polar Electro, Kemple, Finland). Each session included a 10-15 min warm-up at the beginning and 5-10 minutes cool down at the end. The control group was required to keep habitual physical activity and inform the researchers in case of any alteration.

Medication and Diet

The participants were on an oral hypoglycemic regimen which did not change during the study period. The participants were asked to keep their usual diet. They were asked to record food intake the day preceding the measurements and replicate it during the day before the final measurements. They were also asked to record a 3-day (2 weekdays and 1 weekend) dietary recall a week prior to the study period and during the last week. The calorie and macronutrients consumption were assessed to be considered as a covariate in the analysis if there was any significant difference between groups and from pre- to post-test.

Measurements

Before and 48h following the experimental period, body composition was analyzed with the participants wearing minimal clothing using the bioelectrical impedance analyzer (Inbody230. Portable, Frequency: 20 kHz, 100 kHz – Display: 240*320 Color LCD). Blood samples were taken in a fasting state to assess Hb1Ac levels at baseline and after the intervention. HbA1c level was assessed by liquid chromatography (Pishtaz, Tehran, Iran). Neuropathic symptoms were evaluated by Michigan Diabetic Neuropathic Score (MDNS), which includes 46 points clinical score and is used for DPN staging (16). QOL state was assessed by QOL questionnaire that assesses subjective feelings of patients. Quality of sleep was assessed by Petersburg Questionnaire. To assess foot sensation, 10 gr filament was applied to the dorsum of the great toe, and the patients were asked to respond YES when they felt the filament (16).

Statistical Analysis

Data analysis was performed using SPSS software, version 25. Normal distribution of the data was confirmed using Shapiro–Wilk test. Repeated-measures ANOVA was used to determine the intergroup differences. Pre-test and post-test values were also analyzed by paired t test, and independent t test was used to compare the groups at pre-test. Pearson's correlation coefficient was also used to assess the relationship between variables. $P < 0.05$ was considered statistically significant.

Results

Descriptive data are shown in Table 1. Data analysis indicated no significant difference between the groups at baseline ($P > 0.05$). Participants had mild to moderate DPN.

Repeated measures ANOVA indicated that HbA1c significantly decreased in the experimental group compared with the control group ($P = 0.01$). MDNS score also improved in the experimental group throughout the intervention period, which was statistically significant with the control group ($P = 0.001$). MDNS improvement was accompanied by foot sensation improvement, and the monofilament test score increased significantly

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($P=0.01$). Pearson's correlation coefficient also indicated a significant correlation between monofilament score and HbA1c (r = - 0.53 and $P=0.021$) and between MDNS and QOL scores (r = 0.73 and $P=0.01$). Data analysis revealed that QOL and sleep significantly improved following three months of exercise compared with the control group ($P=0.03$ and $P=0.01$, respectively) (Table 2).

Discussion

We found that after three months of aerobic training, HbA1c levels improved, which was coupled with improvement in foot sensation, neuropathic symptoms, and QOL and sleep.

The results regarding reduced HbA1c levels following exercise training are consistent with most studies in this area (9, 17, 18). Metabolic effects of aerobic training have been previously established, especially in patients with metabolic disorders (19). Several mechanisms have been proposed; for instance, glucose uptake in muscles increases during and following exercise because of the increased muscle permeability as a result of contraction (20). In addition, GLUT4 transcription and translocation increase by exercise, which has a direct impact on insulin sensitivity and glucose uptake (20). Although very few studies have recently investigated the effectiveness of exercise on complications of diabetes, particularly DPN, this metabolic effect of exercise training could be promising in this population as hyperglycemia plays a crucial role in the pathogenesis and progression of DPN.

Another finding of the present study was the improvement in MDNS following exercise training. Despite the lack of research on patients with DPN, this finding is consistent with some studies (13, 21). Dixit and colleagues reported that 8-week exercise training improved neuropathic symptoms in people with DPN (21). Kluding et al also found that 10-week combined endurance-resistance training reduced neuropathic pain in patients with diabetes with peripheral neuropathy (13). We also observed that foot sensation assessed by the monofilament test improved by exercise training. Possible causes of improvement in neuropathic symptoms can be attributed to the improvement of underlying factors, including blood glucose and blood circulation to the peripheral nerves. We found that improvement in foot sensation was coupled with HbA1c reduction. Although we did not explore the vascular changes following exercise training in our study, it has been previously reported that patients with neuropathy can benefit from vascular effects of exercise training (22). Thus, these changes brought about by exercise training may explain improvements in neuropathic symptoms. Even though the results were consistent to some extent, this study could be comparable with the aforementioned research in some aspects. For instance, Kluding and colleagues' study was not controlled and randomized, and MNSI was applied by this research group to evaluate the state of neuropathy (13).

Another finding of the study was the improvement in QOL and sleep quality (SQ) in this population following the intervention. This is in line with the results of another study showing that regular exercise over three months improves the QOL in elderly individuals with mild disabilities (23). Several studies have illustrated that moderate exercise training can improve sleep quantity and quality. However, little is known about its effect in

Table 1. Mean ± SD of Body Composition and Calorie Intake

Variables	Groups				*P* Value
	Experimental (n = 12)		Control (n = 12)		
	Pre	Post	Pre	Post	
Age (year)	43 ± 4	-	44 ± 6	-	0.49
Weight (kg)	86 ± 15	85 ± 15	89 ± 11	89 ± 11	0.09
BMI (kg/m^2)	29 ± 5	28 ± 5	29 ± 3	28 ± 2	0.20
Calorie intake (kcal)	2352 ± 224	2392 ± 221	2437 ± 211	2413 ± 168	0.61

P values presented for Time * Group interactions. *P* is presented by baseline comparison for age.

Table 2. Mean ± SD of Variables Throughout the Study

Variables	Groups				*P* Value
	Experimental (n = 12)		Control (n = 12)		
	Pre	Post	Pre	Post	
MDNS	15.2 ± 2.3	12.1 ± 2.1	15.4 ± 2.5	15.3 ± 2.8	0.001
QOL	54.3 ± 7.6	66.4 ± 8.4	51.8 ± 6.4	54.1 ± 8.2	0.03
SQ	8.4 ± 2.0	6.5 ± 1.6	8.9 ± 3.2	8.7 ± 2.7	0.01
Monofilament	4.9 ± 1.5	5.8 ± 1.4	5.1 ± 1.7	5.0 ± 1.6	0.01
HbA1c (%)	8.32 ± 1.41	7.74 ± 1.50	8.61 ± 1.43	8.54 ± 1.83	0.01

Abbreviations: MDNS, Michigan Diabetic Neuropathy Score; QOL, quality of life; SQ, sleep quality.
P values presented for Time * Group interactions.

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patients with DPN. Dixit and co-workers reported that 8 weeks of regular exercise improved the QOL in this group of patients (21). However, they did not assess whether this improved QOL was correlated with neuropathic symptoms. We observed a relationship between the changes in MDNS score and QOL in patients with DPN. We assume that one of the most important possible reasons for improved QOL and sleep with exercise training is the improvement of neuropathic symptoms. Neuropathic pain is an important factor in reducing the QOL in these patients. We also found that following three months of exercise training, the quality of sleep remarkably improved. Neuropathic symptoms in this population are aggravated at night, which could be a cause of sleep disorders and poor SQ (24). Moreover, evidence shows that exercise training improves the quality of sleep through elevating endorphin secretion and energy consumption which facilitates sleep and recovery of the body (25, 26). Thus, we speculate that exercise training can potentially bring about metabolic effects and cause physiological changes that may improve neuropathic symptoms in these patients, which may eventually result in a better QOL and sleep.

Conclusion

Overall, the results of the present study showed that a three-month aerobic exercise training program decreased HbA1c level and improved neuropathic symptoms, QOL and sleep in patients with DPN. There was a correlation between HbA1c and monofilament test score and also between neuropathic symptoms and QOL scores following the intervention. Moderate aerobic training may be recommended as a feasible strategy along with other therapeutic interventions for patients with diabetes and DPN.

Acknowledgment

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Conflict of Interests

The author declares no conflict of interest.

Ethical Approval

The study was approved by the ethics committee in human research (Code: BZMED.REC.1394.153). All the participants were informed about the study procedure, and written consent was obtained from each participant. The study protocol complies with the ethical guidelines of the 1975 Declaration of Helsinki. Besides, the study was registered by the Iranian Registry of Clinical Trials (identifier: IRCT2017012032066N1).

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References

1. Misra A, Singhal N, Khurana L. Obesity, the metabolic syndrome, and type 2 diabetes in developing countries: role of dietary fats and oils. J Am Coll Nutr. 2010;29(3 Suppl):289s-301s. doi: 10.1080/07315724.2010.10719844.
2. Tesfaye S, Selvarajah D. Advances in the epidemiology, pathogenesis and management of diabetic peripheral neuropathy. Diabetes Metab Res Rev. 2012;28 Suppl 1:8-14. doi: 10.1002/dmrr.2239.
3. D'Amato C, Morganti R, Greco C, Di Gennaro F, Cacciotti L, Longo S, et al. Diabetic peripheral neuropathic pain is a stronger predictor of depression than other diabetic complications and comorbidities. Diab Vasc Dis Res. 2016;13(6):418-28. doi: 10.1177/1479164116653240.
4. Naranjo C, Del Reguero L, Moratalla G, Hercberg M, Valenzuela M, Failde I. Anxiety, depression and sleep disorders in patients with diabetic neuropathic pain: a systematic review. Expert Rev Neurother. 2019;19(12):1201-9. doi: 10.1080/14737175.2019.1653760.
5. Argoff CE, Cole BE, Fishbain DA, Irving GA. Diabetic peripheral neuropathic pain: clinical and quality-of-life issues. Mayo Clin Proc. 2006;81(4 Suppl):S3-11. doi: 10.1016/s0025-6196(11)61474-2.
6. Waldfogel JM, Nesbit SA, Dy SM, Sharma R, Zhang A, Wilson LM, et al. Pharmacotherapy for diabetic peripheral neuropathy pain and quality of life: a systematic review. Neurology. 2017;88(20):1958-67. doi: 10.1212/wnl.0000000000003882.
7. Rolim LC, Koga da Silva EM, De Sá JR, Dib SA. A systematic review of treatment of painful diabetic neuropathy by pain phenotype versus treatment based on medical comorbidities. Front Neurol. 2017;8:285. doi: 10.3389/fneur.2017.00285.
8. Cameron NE, Eaton SE, Cotter MA, Tesfaye S. Vascular factors and metabolic interactions in the pathogenesis of diabetic neuropathy. Diabetologia. 2001;44(11):1973-88. doi: 10.1007/s001250100001.
9. Colberg SR, Sigal RJ, Yardley JE, Riddell MC, Dunstan DW, Dempsey PC, et al. Physical activity/exercise and diabetes: a position statement of the American Diabetes Association. Diabetes Care. 2016;39(11):2065-79. doi: 10.2337/dc16-1728.
10. Umpierre D, Ribeiro PA, Kramer CK, Leitão CB, Zucatti AT, Azevedo MJ, et al. Physical activity advice only or structured exercise training and association with HbA1c levels in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2011;305(17):1790-9. doi: 10.1001/jama.2011.576.
11. Nyberg M, Gliemann L, Hellsten Y. Vascular function in health, hypertension, and diabetes: effect of physical activity on skeletal muscle microcirculation. Scand J Med Sci Sports. 2015;25 Suppl 4:60-73. doi: 10.1111/sms.12591.
12. Asensio-Pinilla E, Udina E, Jaramillo J, Navarro X. Electrical stimulation combined with exercise increase axonal regeneration after peripheral nerve injury. Exp Neurol. 2009;219(1):258-65. doi: 10.1016/j.expneurol.2009.05.034.
13. Kluding PM, Pasnoor M, Singh R, Jernigan S, Farmer K, Rucker J, et al. The effect of exercise on neuropathic symptoms, nerve function, and cutaneous innervation in people with diabetic peripheral neuropathy. J Diabetes Complications. 2012;26(5):424-9. doi: 10.1016/j.jdiacomp.2012.05.007.
14. Myers VH, McVay MA, Brashear MM, Johannsen NM, Swift DL, Kramer K, et al. Exercise training and quality of life in individuals with type 2 diabetes: a randomized controlled trial. Diabetes Care. 2013;36(7):1884-90. doi: 10.2337/dc12-1153.
15. Riandini T, Wee HL, Khoo EYH, Tai BC, Wang W, Koh GCH, et al. Functional status mediates the association between peripheral neuropathy and health-related quality of life in individuals with diabetes. Acta Diabetol. 2018;55(2):155-64. doi: 10.1007/s00592-017-1077-8.
16. Feldman EL, Stevens MJ, Thomas PK, Brown MB, Canal N,

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Greene DA. A practical two-step quantitative clinical and electrophysiological assessment for the diagnosis and staging of diabetic neuropathy. Diabetes Care. 1994;17(11):1281-9. doi: 10.2337/diacare.17.11.1281.
17. Borror A, Zieff G, Battaglini C, Stoner L. The effects of postprandial exercise on glucose control in individuals with type 2 diabetes: a systematic review. Sports Med. 2018;48(6):1479-91. doi: 10.1007/s40279-018-0864-x.
18. Jiang Y, Tan S, Wang Z, Guo Z, Li Q, Wang J. Aerobic exercise training at maximal fat oxidation intensity improves body composition, glycemic control, and physical capacity in older people with type 2 diabetes. J Exerc Sci Fit. 2020;18(1):7-13. doi: 10.1016/j.jesf.2019.08.003.
19. Karstoft K, Pedersen BK. Exercise and type 2 diabetes: focus on metabolism and inflammation. Immunol Cell Biol. 2016;94(2):146-50. doi: 10.1038/icb.2015.101.
20. Sylow L, Kleinert M, Richter EA, Jensen TE. Exercise-stimulated glucose uptake - regulation and implications for glycaemic control. Nat Rev Endocrinol. 2017;13(3):133-48. doi: 10.1038/nrendo.2016.162.
21. Dixit S, Maiya A, Shastry B. Effect of aerobic exercise on quality of life in population with diabetic peripheral neuropathy in type 2 diabetes: a single blind, randomized controlled trial. Qual Life Res. 2014;23(5):1629-40. doi: 10.1007/s11136-013-0602-7.
22. Gholami F, Nazari H, Alimi M. Cycle Training improves vascular function and neuropathic symptoms in patients with type 2 diabetes and peripheral neuropathy: a randomized controlled trial. Exp Gerontol. 2020;131:110799. doi: 10.1016/j.exger.2019.110799.
23. Tamari K. Diabetes predicts decreased quality of life among community-dwelling seniors undertaking progressive resistance exercise: an observational study. Aust J Physiother. 2009;55(3):201-5. doi: 10.1016/s0004-9514(09)70082-0.
24. Bansal V, Kalita J, Misra UK. Diabetic neuropathy. Postgrad Med J. 2006;82(964):95-100. doi: 10.1136/pgmj.2005.036137.
25. Driver HS, Taylor SR. Exercise and sleep. Sleep Med Rev. 2000;4(4):387-402. doi: 10.1053/smrv.2000.0110.
26. Li F, Fisher KJ, Harmer P, Irbe D, Tearse RG, Weimer C. Tai chi and self-rated quality of sleep and daytime sleepiness in older adults: a randomized controlled trial. J Am Geriatr Soc. 2004;52(6):892-900. doi: 10.1111/j.1532-5415.2004.52255.x.

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