

Investigating the effect of aerobic exercise on the neuropathy symptoms caused by chemotherapy

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Abstract

Introduction: Currently, there is no effective method to prevent CIPN; and if aerobic exercise combined with drug treatment is more effective than drug treatment alone, the side effects of the drug can be prevented to an acceptable extent by reducing the dose of the relevant drug. Therefore, in the following study, we tried to investigate and compare the effectiveness of two methods of aerobic exercise and drug treatment on the improvement of neuropathy symptoms caused by chemotherapy.

Research materials and methods: In this clinical trial study, the first group of patients received duloxetine (Luxta, Obidi company) at a dose of 30 mg for 6 weeks. The second group received duloxetine at a dose of 30 mg along with aerobic exercise for 6 weeks. At the end of the intervention period, all patients were re-evaluated with EMGMCV of both lower limbs. The study data was analyzed using SPSS version 24 software.

Findings: Two groups of cases (50 people) with an average age of 55.56 ± 4.21 years and controls (50 people) with an average age of 53.76 ± 4.57 years participated in this study. The results of EMGMCV improved significantly in both groups after the intervention, but the two groups did not show a statistically significant difference after the intervention ($P < 0.05$).

Conclusion: Based on the results of the studies and considering that aerobic exercise therapy is simple and available, since there has been no study related to the determination of the effect of combined aerobic exercise that can determine the best and most effective exercise volume affecting neuropathy. And since the existing researches are mostly focused on the effects of exercise on improving performance and neuro-muscular indicators, more clinical studies are needed in this field.

Keywords: Chemotherapy-Induced Neuropathy; Duloxetine; Aerobic Exercise; EMGMCV; Neuro-Muscular

1. Introduction

chemotherapy-induced peripheral neuropathy (CIPN) is a sensory neuropathy that may be associated with motor and autonomic changes of varying severity and duration (1-4). Because of its high prevalence among cancer patients, CIPN is a major problem for these patients and their families as well as their health care providers, especially because there is currently no effective way to prevent CIPN. does not have. In addition, the possibilities of treating this syndrome are very limited (5,6). Various studies have been conducted in Iran and the world to investigate the dimensions of this issue and also to find its prevention and treatment methods. Duloxetine is an antidepressant drug that is used in the treatment of major depression. In several articles, it has been very effective on neuropathic pain caused by diabetes and

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fibromyalgia (7,8). In a study was found that the use of duloxetine is effective in reducing neuropathic pain caused by chemotherapy (9). Also in Gholami et al.'s study in Iran revealed that aerobic exercise may be able to prevent the progression of diabetic PN by improving NCV. It was also suggested that due to the little evidence in this field, the mechanisms related to exercise should be studied in the future (10). Also, in a study, it was determined for the first time that long-term aerobic exercise can be effective from the beginning or change the natural history of neuropathy caused by diabetes (11). This effect was also confirmed in other studies (12, 13). Also, exercise improves other complications and symptoms of cancer such as fatigue, emotional distress and mood changes, pain, Sleep disorders and reduced quality of life are also effective and useful (14). Exercise may also reduce CIPN through its effects on circulation/oxidative stress, inflammation (15, 16), pain inhibitory neurotransmitters (17), endogenous narcotics (18), growth factors, and neuroplasticity (19).

Considering the importance of the subject and the high prevalence of cancer in Iran, there is still a need for more studies in this field. Therefore, in the following study, we tried to investigate and compare the effectiveness of two treatment methods, aerobic exercise and drug treatment, on the improvement of neuropathy symptoms caused by chemotherapy. It is hoped that the results of this research will be helpful in improving the health of our beloved Iran.

2. Methods

In this study, after obtaining the code of ethics IR.TBZMED.REC.1400.621, patients with cancer referred to Army Teaching-Therapeutic Hospital (Imam Reza) who have symptoms of peripheral neuropathy caused by chemotherapy were examined. The number of study samples is considered due to time and resource limitations and by reviewing previous studies (10) considering 15% drop in patients in 2 groups and 50 samples in each group. At first, the researcher explained the objectives of the study to the patients and assured them that the ethical principles of the research will be observed during the study, and then a written consent form was obtained from the patients. Patients were evaluated with EMGMCV of both lower limbs. Patients were referred to a rehabilitation and physical medicine specialist and the severity of neuropathy was determined using the nerve-muscle strip test. Patients were divided into 2 groups according to random table.

In the first group, patients received duloxetine (Luxta, Obidi company) with a dose of 30 mg for 6 weeks. The second group received duloxetine at a dose of 30 mg along with aerobic exercise for 6 weeks. The movement intervention was based on the Lebed method, and the sessions were recorded by the researcher and the therapist and guided by the certified trainer of the Lebed method. The duration of this program was 6 weeks, with 2 sessions per week for the first 3 weeks and one session per week for the other 3 weeks, a total of 9 sessions. The duration of this program was designed so that patients who are undergoing radiation or chemotherapy and may miss sessions due to fatigue or side effects, can still attend enough sessions to benefit from the program. Program expectations were clearly stated in the first class and subsequent sessions. The content of the classes includes "take your time to improve your posture, stop if something hurts, don't worry about coordination, and most importantly, have fun." Chairs were available and could be done sitting on a chair if the participant felt weak or tired. Warm-up (10-15 minutes) Each session began with breathing and stretching designed to improve lymphatic drainage.

This included deep breathing, head and neck stretches, shoulder rotations, upper body contractions, side-to-side arm extensions, trunk lengthening, and large arm circles. This was usually done in a circle with percussion music set for these movements. Bilateral stretching exercises were followed in a standing position using a chair for support. For the first few weeks, lower body movements alternated with upper body movements. Core exercises of shoulder, elbow and wrist upper limb movements were performed bilaterally with music, with 4 or less repetitions per side. Lower body movements, such as side-to-side twists, walking around in different attitudes, and chair balance exercises, are introduced to provide a break from upper body activities and increase energy flow.

At the end of the intervention period, all patients were re-evaluated with EMGMCV of both lower limbs. Nerve conduction speed and action potential amplitude were measured by EMG device model II Myto made in Italy. Subjects were placed lying down on the bed and nerve measurements were taken from their right leg. To measure nerve conduction velocity and peroneal nerve action potential amplitude, the first surface electrode was placed in the ventral area of the extensor brevis muscle of the toes and the second electrode was placed in the fifth metatarsal joint or on the fifth toe. In the case of the tibial nerve, the first electrode was placed one centimeter from the inferior posterior part of the navicular bone prominence in the middle part of the foot and the second electrode was placed in the metatarsal joint or the distal part of the first toe. In the case of the sural nerve, the first electrode was placed in the lateral part of the ankle and the second electrode was placed near the lateral part of the ankle.

3. Results

In the present study, 100 patients participated in 2 case groups (50 people) and control groups (50 people). The case group included 23 men and 27 women and the control group included 27 men and 23 women. The average age of the case group was 55.56 ± 4.21 years and the average age of the control group was 53.76 ± 4.57 years. Before the intervention, EMGMCV results in the case group were 14.0% Mild, 34.0% Moderate and 52.0% Severe. In the control group, 10.0% Mild, 48.0% Moderate and 42.0% Severe. According to the results of Chi-square test, there was no statistically significant difference (table 1).

After the intervention, EMGMCV results in the case group were 58.0% Mild, 26.0% Moderate and 16.0% Severe. In the control group, 58.0% were mild, 34.0% were moderate and 8% were severe. According to the chi-square test, there was no statistically significant difference between the two groups. However, according to the results of the Wilcoxon test, significant improvement was observed in both groups compared to before the intervention (P value = 0.001).

Table 1 Characteristics of EMGMCV in two groups of cases (aerobic exercise + drug) and control (drug) before and after the intervention

		EMGMCV	person	percentage	P value
Before intervention	Case group	Mild	7	14.0	0.357
		Moderate	17	34.0	
		Severe	26	52.0	
	Control group	Mild	5	10.0	
		Moderate	24	48.0	
		Severe	21	42.0	
After intervention	Case group	Mild	29	58.0	0.393
		Moderate	13	26.0	
		Severe	8	16.0	
	Control group	Mild	29	58.0	
		Moderate	17	34.0	
		Severe	4	8.0	

4. Discussion

In the present study, EMGMCV results improved significantly in both groups after the intervention, but the two groups did not show a statistically significant difference after the intervention. The benefits of aerobic exercise in people with peripheral neuropathy can be attributed to several cellular and molecular mechanisms. It has been shown that aerobic exercises cause nerve stimulation, reduce systemic inflammation, reduce oxidative stress and improve glucose metabolism, which can reduce the symptoms of peripheral neuropathy (20-23). Evidence about the cellular and molecular mechanisms of aerobic exercise in diabetic peripheral neuropathy emphasizes the importance of exercise in the management of neuropathy. Overall, these findings provide important insights into the cellular and molecular mechanisms underlying the beneficial effects of aerobic exercise in people with diabetic peripheral neuropathy (24,25). A better understanding of these mechanisms is very important in the development of exercise interventions aimed at improving the health and quality of life of people with peripheral neuropathy, especially considering the increasing prevalence of cancer worldwide (26-30).

Duloxetine drug by inducing and stimulating mechanisms can lead to an increase in serum zinc, which in turn can be effective on the pathogenesis of the disease or its recovery. In the conducted studies, the amount of zinc in diabetic neuropathy patients has decreased, and the occurrence of peripheral neuropathy can be prevented by prescribing zinc (31). In terms of evaluating the pain level of the patients using a numerical-visual scale, data analysis showed that the reduction in the pain level of the duloxetine group was significantly higher (32). In the study conducted by Simpson et

al., the effectiveness of gabapentin administration in peripheral neuropathy has been shown (33-36). Several studies investigated the effectiveness of duloxetine and compared it with other drugs. A meta-analysis study showed that duloxetine is more effective in treating neuropathic pain compared to other drugs such as pregabalin and gabapentin (37,38). The study conducted by Wasen et al showed that duloxetine is well tolerated by most patients and regardless of the patient's age, this drug is effective for treating neuropathic pain (39-43). Another study conducted by Kiaj Dasiz and colleagues in America showed that duloxetine is an effective drug for the treatment of neuropathic pain, which can help control neuropathic pain (44-47). According to a study conducted in England, it is effective and cost-effective to use duloxetine to improve neuropathic pain (48-52).

A research entitled the firing rate of the maximum motor unit during isometric resistance training in men concluded that four weeks of resistance training causes a significant increase in the action potential of the nerve (34, 48-52). Another study entitled the effect of eight weeks of regular sports activity including aerobic and strength training, they came to the conclusion that the speed of nerve conduction and the amplitude of the potential of the inferior long nerves do not change significantly as a result of training (53, 54). In their research titled Neuromuscular adaptations in human palm muscles following resistance training and staying still, Sel et al concluded that five weeks of resistance training does not have a significant effect on nerve action potential (55,56). The reason for the difference in these results can be attributed to the difference in the training protocol, which is that the duration of resistance training in these studies was short.

Neurological parameters such as nerve conduction velocity, electromyography, motor unit recall and Hoffman's reflex are all possible to change in response to sports activity, and the possible mechanisms of performance improvement as a result of exercise include changes in the temporary displacement of muscle activation for greater motor efficiency, preferential recall of motor units. Faster, faster nerve firing, calcium ion release, Ca ATPase increase and motor neuron excitability (57-62). One of the factors of increasing the amplitude of the action potential can be increasing the excitability of the sarcolemma after exercise. This phenomenon may be caused by the increase in sodium pump activity due to the exercise program. It has been shown that the regulation of sodium and potassium ATPase levels are both largely affected by exercise stimulation, although changes in intracellular water content and subcutaneous fat tissue can also affect this factor (31,34).

5. Conclusion

Due to the existence of contradictions in the results of studies, factors such as study design, duration of treatment, demographic characteristics and other confounding variables can affect the results of the study. Therefore, more studies are needed to better understand the underlying mechanisms in the effect of aerobic exercise on neuropathy caused by cancer. We aim to provide a roadmap for future therapeutic targets in the management of peripheral neuropathy.

Compliance with ethical standards

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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