



Sensorimotor Training on Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer

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Abstract

Cancer female patients suffering from chemotherapy induced peripheral neuropathy (CIPN) exhibit motor and sensory impairments leading to decreased balance. The sensorimotor training may correct these impairments and hence improve function. This study was to assess how sensorimotor training program affected neuropathy symptoms and functional activities in breast cancer female patients with CIPN. Sixty breast cancer female patients complaining from CIPN participated in this study. Their ages ranged from 30 to 50 years. They were selected from Al-Haram hospital and National Cancer Institute, Cairo University. Patients were randomly and distributed into two equal groups in number control and study groups. Both groups received chemotherapy and medical supplements. In addition the study group received sensorimotor training program; 2 times/week for 12 weeks. Visual analogue scale (VAS) was used to assess neuropathic pain and chemotherapy induced peripheral neuropathy assessment tool was used to assess neuropathy symptoms and functional activities, before and after the end of 12 weeks. There was a significant decrease in VAS of study group 74.59% and control group 31.71%, symptom experience of study group 55.22% and interference items of study group 66.46%, symptom experience of control group 22.17% and interference items of control group 34.82% post treatment compared with that pre-treatment in study and control groups ($p < 0.001$). While, comparison between groups post treatment revealed a significant decrease in VAS, symptom experience and interference items of study group compared with that of control group ($p < 0.001$). Sensorimotor training improves neuropathy pain, symptoms and function in cancer female patients complaining from CIPN. So, sensorimotor training can be implemented in the management of cancer patients treating with chemotherapy to prevent or decrease their symptoms and disabilities.

Keywords: Breast cancer, Chemotherapy, Peripheral neuropathy, Sensorimotor training

Full-length article

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1. Introduction

Chemotherapy is the use of extremely potent and low molecular weight chemotherapeutic medications to target tumor cells and stop them from multiplying, but not without serious side effects[1]. Of these, Chemotherapy-induced peripheral neuropathy (CIPN) is the common side effect that mainly affects sensory nerve fibers and also motor and autonomic ones[2]. This is because chemotherapy causes damage to mitochondria and neuronal cell bodies in the dorsal root ganglia, as well as axonal toxicity, axonal membrane ion changes, channel malfunction and central sensitization[3]. The CIPN affects between 30-68% of patients based on the duration from chemotherapy[4]. The symptoms of CIPN include paresthesia, numbness, pain, muscles weakness that starts distally and progress proximally with dose

accumulation[5]. Moreover, 82% of breast cancer patients receiving chemotherapy cycle had reduced muscle strength, endurance and life quality[6]. In addition, they had increased rate of falls and disability[7].

The CIPN is commonly treated with drugs as steroids and opioids[8]. However, these treatments are directed mainly to relieve pain but not weakness, imbalance, and disability which are common and serious. So, other treatments are needed. Exercises as sensorimotor training, balance training and strengthening exercise improve function, balance, neuropathic symptoms, fatigue, and life quality in cancer patients including breast cancer[10-9]. There is lack in the knowledge about role of sensorimotor training on CIPN in breast cancer⁽¹⁾. So, the purpose of the study was to determine the sensorimotor training effects on

neuropathy symptoms and functional activities after chemotherapy in breast cancer female patients complaining from CIPN.

2. Subjects and Methods

2.1. Study design

A prospective, randomized, single-blind, pre-post test controlled trial was planned for this study. It was approved by the research ethics committee of faculty of physical therapy, Cairo University before the beginning of the study (P.T.REC/012/003927). The study took place between (October 2022) and (January 2023).

2.2. Randomization

The patients were randomly divided into 2 equal groups in number using the closed envelope method. The therapist made 60 closed envelopes, each with a card labelled with either controlled or study group. Finally each patient was asked to draw a closed envelope indicating whether she had been assigned to the control or study groups

2.3. Subjects

Sixty female patients who treated with neurotoxic potential chemotherapy and complained from chemotherapy induced peripheral neuropathy (CIPN) participated in this study. The participants were selected from National Cancer Institute-Cairo University, and Al Haram Hospital. Both groups received medical supplements like melga and dipovit injection.

In addition, the study group performed a sensorimotor training program for 2 times/week for 12 weeks. The patients participated in this study after signing their informed consent form before data collection. Female patients were included if they had breast cancer and received chemotherapy drugs like taxanes and carboplatin through the previous 6 months, aged between 30 and 50 years, and reported at least one of the neuropathic symptoms according to chemotherapy induced peripheral neuropathy assessment tool (CIPNAT)⁽¹²⁾. They were excluded if they had respiratory or heart problems, marked skeletal deformity or bone metastasis, cognition issues, diabetes, neuritis, vitamin B deficiency or cervical and lumbar radiocluopathy.

All female patients were evaluated by the same physician and received the same medical and traditional physical therapy treatment.

2.4. Measurement Procedures

All patients completed history talking including their name, age, address, occupation, weight, height, body mass index. In addition they were asked about the progress of their breast cancer like onset of breast cancer, duration, number of chemotherapy cycles, type of chemotherapeutic drugs like taxanes and carboplatin and any medical supplements were taken.

Measurements were taken at the beginning of the study (pre-treatment) and after 12 weeks of treatment (post treatment). All patients were instructed to report any side effects during the management. All patients were informed about the assessment and treatment procedures before starting of the study to gain their confidence and cooperation during the study course.

2.5. Assessment procedures

2.5.1. Visual analogue scale (VAS)

Patients were asked to mark a point on a 100 mm line with "No pain" and "Worst imaginable pain at its ends" that best represented their level of neuropathic pain. Distance from "No pain" end to the marked point was measured by a ruler as a VAS score.

2.5.2. Assessment of neuropathy symptoms and functional activities

Neuropathy symptoms and functional activities were assessed by CIPNAT for each patient in both control and study groups at the starting of the study and after 12 weeks of the treatment program. CIPNAT is consisting of 50-items in two sets including symptom experience and interference items. Each patient was carefully instructed about the CIPNAT and was given a sufficient time to complete it. It showed high reliability and validity as a comprehensive assessment of peripheral neuropathy in cancer patients⁽¹³⁾.

2.5.3. Evaluation of symptoms experience items score

The symptoms experience items assessed the existence, severity, distress, and frequency of nine neuropathic symptoms, which the patient felt since she received her chemotherapy cycles. These symptoms included numbness in the hands, numbness in the feet, tingling in the hands, tingling in the feet, sensitivity to cold temperatures, nerve pain, muscle/joint aches, muscle weakness, and loss of balance. To calculate symptom items score, each patient was asked to answer about the occurrence of 9 symptoms by yes or no. "Yes" indicated a score of 1 and no indicated a score of 0. For each yes response, each patient was asked to answer 3 additional items that evaluated degree, distress and frequency of every symptom using a rating scale from 0 to 10. The range of this score was from 0 to 270. By adding the range of occurrence (0-9) to the range of the 3 additional items mentioned above (0-270), so the range of scores would be from 0 to 279. Higher scores corresponded to more severe, distressing, or frequent neuropathic symptoms⁽¹²⁾.

2.5.4. Evaluation of the interference items score

The interference items assessed the neuropathic symptoms interference with daily activities. These items assessed how much the neuropathic symptoms interfere with the following activities including walking, picking up objects, driving, dressing, holding onto objects, Participating in hobbies, working, sleeping, exercising, enjoying life, sexual activity, relationships with other people, writing, and usual household. To calculate the interference items score, each patient was asked to express the effect of CIPN symptoms on her functional activities for 14 interference items, using a numeric rating scale of 0 to 10 for each item. The scores ranged from 0 to 140. Higher scores on the interference item corresponded to poorer functional status⁽¹²⁾.

2.5. Treatment procedures

2.5.1. Medical treatment

All patients in both groups received neurotoxic potential chemotherapy through the previous six months like Taxanes and Carboplatin and also took medical supplements after chemotherapy cycles like Melga and Depovit injection. All patients in both control and study group were instructed to keep their level of daily activities.

2.5.2. Sensorimotor training program:

a. Sensory re-education/retraining (30-40 minutes)

a1- Vibration somatosensory stimulation

Vibrations at the foot or other portions of the lower extremity was utilized to aid ankle dexterity in high-precision or to improve sensory deficits in their toes⁽¹⁴⁾. All patients in group (A) received vibration somatosensory stimulation for 10 minutes / session, 2 sessions a week for 12 weeks. Sessions were performed while the patient was supine lying on a bed with his affected feet bared skin and rested on the bed. Then a vibrator was applied on patient's volar aspect of the foot.

a2. Light and rough touch stimulation

All patients in group (A) also received light and rough touch somatosensory stimulation (using soft brush and sand paper, respectively) for 20 minutes every session 2 sessions a week for 12 weeks. Stimulation was performed while the patient was supine lying on a bed with his affected feet bared skin and rested on the bed. Then a soft brush and sand paper were applied gently on patient's volar aspect of foot. The tips of the brush and sandpaper were angled at 30 degrees to the skin surface to deliver light and harsh touch stimulations⁽¹⁵⁾.

a3. Cryotherapy-Brief

Ice was used to facilitate a muscle response, which used a combination of coolness and pain sensation to produce the desired response⁽¹⁶⁾. Ice was applied over sole of the foot to reduce neuropathic pain.

2.6. Selected balance training program

This program was described according to the previous researches and the American cancer society guidelines. The selected balance training program consisted of warming up phase, active phase including the balance training program and cool down phase. Each patient in group (A) was carefully instructed about the benefits of balance training and the procedures of each exercise to gain their confidence and cooperation during the treatment. They were asked to wear light cotton clothes, and to evacuate the bladder before starting of the treatment session.

The program of balance training consisted of the following phases:

2.6.1. Warm-up phase

Each patient was instructed to do march in place exercise. She was asked to stand with her back straight, her feet apart, and both arms beside her sides. She was asked to flex her right shoulder forward and flex her left knee at the same time, and then she extended the previous joints and repeated the exercise on the opposite side.

She was asked to keep alternating movements for 30 seconds and natural for 30 seconds. She was advised to keep her breathing pattern steady and natural until the exercise will be completed. This exercise was simple and safe for breast cancer patients, which would not put strain on their joints.

2.6.2. Active phase

2.6.3. Stretching exercise (10 minutes)

Each static stretch exercise was maintained for 20-30 seconds and repeated for 3 times with 30 seconds rest in between. Both sides were treated.

2.6.4. Hamstring Muscle stretch

Each patient was asked to sit on the plinth, in a long sitting position with both knees extended and ankles dorsiflexed. The patient was asked to bend her trunk forward, trying to touch her toes with her fingers.

2.6.5. Hip flexor muscle stretch

Each patient was asked to sit as close to the plinth's edge as feasible. She was instructed to draw her knees to her chest and then slowly slide her back backwards on the plinth. One lower limb was released, enabling the hip to extend and hang it off the edge of the plinth. The therapist placed one hand on the flexed limb, and the other hand above the knee of the hanged limb pushing it downward to allow more stretching.

2.6.6. Calf muscles stretch

Each patient was asked to sit in a long sitting position. The therapist stood at the level of the leg being stretched. She grasped the patient's heel with one hand, maintaining the subtalar joint in a neutral position, and placed her forearm along the planter surface of the patient's foot, and stabilized the knee joint with the other hand. The therapist pulled the calcaneus in an inferior direction with her thumb and fingers, and then she applied a gentle pressure in a superior direction immediately proximal to the heads of the metatarsals.

2.7. Active free exercise (10 minutes)

Patients performed active free exercise for the first 2 weeks. Each exercise was done with 10 repetitions for 2 sets and 30 seconds rest was given between each set of exercise. Both sides were treated.

2.7.1. Active free exercise for knee extensors muscles

Each patient was instructed to sit on the edge of the plinth with her back straight, hands rested on the plinth, and both hips and knee joints flexed at 90 degrees. The patient was asked to dorsiflex the ankle joint, extend the knee joint of the left leg, holding this position, then relaxed and returned to the starting position.

2.7.2. Active free exercise for hip abductor muscles

Each patient was asked to assume side-lying position, with knee and hip joints of the bottom leg slightly flexed. However, the top leg was kept at full extension. Each patient was asked to raise the top leg upward throughout the full range of motion, holding this position, then relaxed and returned to the starting position.

2.7.3. Active free exercise for hip extensors muscles

Each patient was asked to assume prone lying position, with her arms beside her body, both legs were extended and her feet outside the plinth. The patient was asked to raise her left leg upward, as much as she could, while keeping the knee extended, holding this position, then relaxed and returned to the starting position.

2.7.4. Strengthening exercise (10-15 minutes)

Strengthening exercise was performed for the remaining 10 weeks. Each patient performed the exercise 10 repetitions for 2 sets. She maintained each contraction for at least 6 second with 6 seconds rest in between contractions. 30

seconds rest was given between each set of exercise. Both sides were treated.

2.7.5. Knee extensors strengthening exercise

Each patient was instructed to sit on a plinth with her back straight, hands rested on the plinth, both hips and knee joints flexed to 90. The sandbags were put on and tied carefully at the lower part of the tibia. The patient was asked to dorsiflex the ankle joint and to fully extend the knee joint of the left leg.

2.7.6. Hip abductors strengthening exercise

Each patient was asked to lie in a side-lying position on the plinth, with knee and hip joints of the bottom of the lower limb slightly flexed. However, the top of the lower limb was kept at full extension and in mid-position. The sandbag was put on and tied carefully at the lower part of tibia at the top lower limb. Each patient was asked to raise the top lower limb upward, without moving the rest of her body.

2.7.7. Hip extensors strengthening exercise

Each patient was asked to assume prone lying position, with her arms beside her body, both legs were extended and her feet outside the plinth. The sandbag was put on and tied carefully at the lower third of tibia. Each patient was asked to raise her left leg upward, as much as she could, while keeping the knee extended.

2.7.8. Rhomboids muscle strengthening

Each patient was instructed to assume stride standing position. The patient was asked to hold one dumbbell in each hand with both elbows and shoulders joints were flexed. Then, she was asked to slowly pull her arm backwards with horizontal abduction of both shoulder joints, tightening her rhomboids muscles by squeezing her shoulder blades together.

2.7.9. Trapezius muscle strengthening

Each patient was asked to assume prone lying position, with her arms beside her body, both legs were extended and her feet outside the plinth. The patient was asked to raise her head and upper trunk upward as much as she could.

2.7.10. Erector spinae muscle strengthening

Each patient was asked to lie in a crock lying position with both feet rested on the plinth, and her arms beside her body. Patient was asked to press the feet on the plinth and lift her buttocks off the plinth as much as possible.

2.8. Balancing exercises (50-60 minutes)

Balance training was performed for each patient 2 sessions/week for 12 weeks. Total sessions for each patient were 24 sessions. Each session lasted for 50-60 minutes. It included the following;

2.8.1. Sit to stand on a chair

Each patient was instructed to sit down on a chair with her arms crossed on her chest, and feet rested on the ground and apart from each other. The therapist stood in front of the patient. The patient was asked to stand up keeping her back straight and her eyes looking forward, holding this position, then relaxed and returned to the starting position. This exercise was performed for 10 to 15 repetitions.

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2.8.2. Practice standing on one foot

Each patient was asked to stand in an erect position in front of mirror and her back straight, both arms beside her body, head was directed toward the ceiling, and her eyes were opened and looked forward in the first 2 weeks of the study program, then she practiced it with closed eye in the remaining 10 weeks. The therapist stood behind the patient to protect the patient from losing her balance during the exercise. The patient was asked to stand on one limb and lift the other foot from the ground by flexing her knee joint, holding this position as she could then relaxed and returned to the starting position. The exercise was performed to the other leg, and was repeated for 10 to 15 repetitions for each leg.

2.8.3. Heel-to-toe walking

Each patient was asked to stand with her back erect and arms beside her body. The therapist stood beside the patient along the exercise. Each patient was asked to walk putting one foot in front of the other one, with the heel and toes should touch or almost touch each other. After walking 10-20 steps forward, she was asked to reverse and walk backward toe to heel. This exercise was repeated for 10 times with 30 seconds rest after 5 repetitions.

2.8.4. Perturbation exercise in different directions

Each patient was instructed to assume stride position, the arms beside her body, and her feet apart from each other. The patient was asked to keep her body balanced as she could, while the therapist pushed the patient's trunk at her shoulder level in anteroposterior and mediolateral directions. Then the exercise was repeated with variations in the starting position of the patient: once with a one-foot step forward and the other time with the same footstep backward.

2.8.5. Reaching forward exercise

Each patient was instructed to assume stride standing position, with her back straight, one arm beside the wall with shoulder flexed to 90 degrees and elbow extended, while the other hand beside her body. The patient was asked to reach forward with her stretched arm as much as possible without moving her foot from their place. This exercise was repeated for 10 times for each arm.

2.8.6. Walking in figure of "8" exercise

Each patient was instructed to assume stride standing position, with her back straight, and both arms beside her body. The therapist put 2 sandbags on the floor about 3 to 4 feet apart. The patient was asked to walk around these 2 sandbags in a figure of 8 patterns for 30 seconds and then relaxed for another 30 seconds. This exercise was repeated for 5 times.

2.8.7. Cooling down phase (5 minutes)

Each patient was asked to breathe deeply while practicing marching in place as mentioned in warm up phase for 5 minutes.

2.9. Sample size calculation

Sample size calculation was performed using G*POWER statistical software (version). It showed that the needed sample size for this study was thirty subjects for each group.

Input: Tail(s)=Two, Effect size $d=0.50$, Sample size group 1=30, Sample size group 2=30.

Output: Noncentrality parameter=1.9364917, Critical $t = 0.37368$, α error prob =0.7 Power, (1- β error prob) =0.95.

2.10. Statistical analysis

Unpaired t-test was conducted for comparison of age and chemotherapy cycles between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to test the homogeneity between groups. Unpaired t-test was conducted to compare VAS and CIPNAT between study and control groups. Paired t-test was conducted for comparison between pre and post treatment. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

3. Results and Discussion

3.1. Subject characteristics

Table (1) showed the subject characteristics of study and control groups. There was no significant difference between groups in age and chemotherapy cycles ($p > 0.05$).

3.2. Effect of treatment on VAS and CIPNAT

3.2.1. Within group comparison

There was a significant decrease in VAS, symptom experience and interference items post treatment compared with that pre-treatment in study and control groups ($p < 0.001$). The percent of change in VAS, symptom experience and interference in study group was 74.59, 55.22 and 66.46% respectively, while that in control group was 31.71, 22.17 and 34.82% respectively. (Table 2).

3.2.2. Between groups comparison

There was no significant difference between groups pre-treatment ($p > 0.05$). Comparison between groups post treatment revealed a significant decrease in VAS, symptom experience and interference items of study group compared with that of control group ($p < 0.001$). (Table 2).

Chemotherapy and its medications could lead to a loss of balance, neuropathy, muscle weakness, and impaired life quality^(17, 18, 19, 2) So, This study aimed to assess effects of sensorimotor training program on neuropathy symptoms, balance and functional activities in breast cancer female patients with CIPN. The findings of this research revealed a highly significant improvement in neuropathic pain and the symptom experience and interference items score after treatment in both groups. However, the improvements were significantly higher in the study group that received sensorimotor training program. The percent of change in VAS, symptom experience and interference in study group was 74.59%, 55.22% and 66.46% respectively, while that in control group was 31.71%, 22.17% and 34.82% respectively.

These findings indicated additional improvements in neuropathy pain and symptoms, balance control and functional activities in the cancer female patients complaining from CIPN following 3 months sensorimotor training program. Improved balance, function, and neuropathic symptoms after sensorimotor training can be explained by its beneficial effects in reducing side effects and

improving fatigue and patient's QoL before, during, and after the treatment of cancer^(20,21,22). Sensory re-training repetitive neural input that helps patients meaningfully interpret the altered neural impulses reaching his conscious level after the altered sensation area has been stimulated⁽²³⁾. It can produce plastic changes in the somatosensory cortex which can compensate, in part, for some of the impairments associated with nerve injury⁽²³⁾. It aids in the recovery of sensibility⁽²⁴⁾.

In agreement with the results of the current study, Vollmers et al. (2018) found that 6 weeks of sensorimotor exercises improve strength and balance in breast cancer patients undergoing neurotoxic chemotherapy (Paclitaxel). As well, Streckmann et al. (2019) studied the effects of sensorimotor training (SMT) (twice a week for 6 weeks) on patients with CIPN and found that SMT is superior to the oncological treatment regarding the tendon reflexes, and a tendency regarding the subjective report of symptoms.

Moreover, Müller et al. (2021) reported that SMT (3×/week for a total of 105 min/week during 20 weeks of chemotherapy) alleviate subjectively perceived sensory CIPN symptoms in the feet and other clinically relevant cancer therapy-related outcomes at 3 weeks. Furthermore, Reitz et al. (2022) documented that 4 weeks of SMT improved strength, mobility, and physical activity in pediatric oncology.

Findings of the current study came in line with Toftagen et al., (2012) who demonstrated that balance and strengthening exercise were safe and effective ways to prevent falls. It also enhanced lower extremity balance and strength in adults over the age of 50, who were at high risk of falling.

In addition, Schwenk et al., (2016) supported the current study and reported that older cancer patients can significantly improve their postural balance with properly designed sensor-based exercise training. Also, Kneis et al., (2019) found that combining balance and endurance training improves patients' functional activities, cardiorespiratory fitness and decrease pain as well as sensory symptoms associated with CIPN. In line with the present study, Lin et al., (2021) reported that a combined aerobic, resistance, and flexibility exercise program is beneficial during chemotherapy in improving fitness and QoL.

In contrast to the findings of the current study regarding beneficial effects of SMT on CIPN symptoms, Wu et al. (2022) found that exercises did not improve CIPN symptoms. In addition, a systematic review and meta-analysis study of randomized controlled trials reporting exercise intervention in cancer patients with chemotherapy-induced peripheral neuropathy showed that there was no evidence that exercise intervention could improve CIPN symptoms (Guo et al., 2023).

Breast cancer women treating with chemotherapy can be treated with sensorimotor training to reduce their symptoms and improve their balance and function.

This study is limited by including only females. However, breast cancer affects mainly women. Other limitation is lack of long term follow-up.

Table 1. Comparison of subject characteristics between study and control groups

	Study group	Control group	MD	t- value	p-value
	Mean ± SD	Mean ± SD			
Age (years)	40.73 ± 5.86	39.20 ± 3.96	1.53	1.18	0.24
Chemotherapy cycles	5.36 ± 1.09	5.23 ± 1.04	0.13	0.48	0.63

SD, standard deviation; MD, mean difference; p value, probability value

Table 2. Mean VAS and CIPNAT pre and post treatment of study and control groups

	Study group	Control group	MD	t- value	p value
	Mean ± SD	Mean ± SD			
VAS					
Pre treatment	8.50 ± 1.04	8.20 ± 0.96	0.3	1.15	0.25
Post treatment	2.16 ± 0.87	5.60 ± 1.07	-3.44	-13.61	0.001
MD	6.34	2.6			
% of change	74.59	31.71			
t- value	33.73	14.19			
	<i>p = 0.001</i>	<i>p = 0.001</i>			
CIPNAT					
Symptom experience					
Pre treatment	203.30 ± 10.73	198.80 ± 11.08	4.5	1.59	0.11
Post treatment	91.03 ± 14.87	154.73 ± 19.35	-63.7	-14.29	0.001
MD	112.27	44.07			
% of change	55.22	22.17			
t- value	68.28	17.47			
	<i>p = 0.001</i>	<i>p = 0.001</i>			
Interference items					
Pre treatment	104.23 ± 3.35	105.30 ± 4.40	-1.07	-1.05	0.29
Post treatment	34.96 ± 6.05	68.63 ± 7.91	-33.67	-18.51	0.001
MD	69.27	36.67			
% of change	66.46	34.82			
t- value	76.79	20.92			
	<i>p = 0.001</i>	<i>p = 0.001</i>			

SD, standard deviation; MD, mean difference; p-value, probability value

4. Conclusion

Sensorimotor training, added to chemotherapy, improves neuropathic pain and symptoms, balance control and functional activities in the cancer women complaining from CIPN, more than chemotherapy alone. So, sensorimotor training can be implemented in the management of cancer patients treating with chemotherapy to prevent or decrease their symptoms and disabilities.

5. Recommendations

Authors of this study recommend repeating this study using larger sample size. They also recommend doing more studies that use different methods of evaluation of peripheral neuropathy, that evaluate the electrotherapy effect on chemotherapy-induced peripheral neuropathy, and that determine the impact of radiotherapy treatment on Functional activities, balance, quality of life in cancer survivors.

Acknowledgment

The authors thank the patients who participated in this study and the physiotherapists at El Bakari family medicine centre for their active participation, cooperation, and unlimited support throughout this work.

Financial support and sponsorship

Nil

Conflicts of interest

Nil

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