EFFECT OF BALANCE TRAINING ON FUNCTIONAL ACTIVITIES AND SYMPTOMES OF CHEMOTHERAPY-INDUCED PERIPHERAL NEUROPATHY

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ABSTRACT

Purpose of the study: The aim of this study was to evaluate the effect of balance training program on functional activities and symptoms of chemotherapy-induced peripheral neuropathy in breast cancer women.

Methods: A total of 40 breast cancer women participated in the study. Their age was 40-50 years and their body mass index ranged from 25 to 34.9 kg/m². They were randomly distributed into two equal groups. Both control and study groups received neurotoxic potential chemotherapy including paclitaxel and docetaxel for at least 4 cycles within the previous 6 months and continued to receive their dose as an adjuvant therapy. In addition, the study group received a balance training program for 50-60 minutes, 2 sessions/week for 12 weeks. Each patient was assessed using functional reach test and chemotherapy-induced peripheral neuropathy assessment tool (CIPNAT) before and after 12 weeks of the intervention protocol.

Results: There was no significance difference (p>0.05) in the functional reach distance and interference items score and a significant increase (p<0.05) in the symptom experience items score of the control group post-treatment. However, there was a significant increase (P=0.0001) in the functional reach distance and a significant decrease (P=0.0001) in the interference items score and symptom experience items score of the study group post-treatment. Compared to the control group, the study group showed more significant increase (P=0.0001) in the functional reach distance and a significant decrease (P=0.0001) in the interference items score and symptom experience items score.

Conclusion: The balance training program is beneficial for improving the functional activities, and attenuating symptoms of chemotherapy-induced peripheral neuropathy in breast cancer women.

Key Words: Breast cancer, Chemotherapy-induced peripheral neuropathy, Balance training.

I. INTRODUCTION:

Chemotherapy-induced peripheral neuropathy (CIPN) is the most common neurological and clinically relevant side effect of many commonly used chemotherapeutic agents (1). Patients frequently suffer from progressive, enduring, often irreversible, and dose-limiting nerve damage during the administration of antineoplastic drugs (2).

Approximately 30–40% of patients treated with neurotoxic chemotherapy develops CIPN. As cancer survival rates continue to improve, the prevalence of CIPN late effects will likely increase (3). A systematic review found

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that the CIPN prevalence after receiving chemotherapy was 68.1% in the first month, 60.0% at the third month, and 30% at the sixth month or more (4). The symptoms associated with CIPN often improves or completely resolves after the end of chemotherapy treatment, but there is about 30-83% has persistent neuropathy (4).

The symptoms of CIPN include unusual sensations (paresthesias), numbness, pain, and weakness of the muscles in the feet and hands (5). CIPN affects the distal sites first, and accumulative doses of chemotherapy lead to increase symptoms severity and affect more proximal areas (4).

Chemotherapy causes a degeneration of peripheral sensory and motor nerves. Changes in the sensory pathways of the spinal cord, thalamus, and regions of the cortex such as the somatosensory cortex and the insula. These changes may exacerbate symptoms of peripheral nerve damage (6).

Deficits in sensory and motor nerves results in sensory disturbances, balance problems or weakness of muscles leading to inappropriate proprioceptive feedback, impaired postural control, and fall risk (7). CIPN is often sensory-predominant with pain and may lead to long-term morbidity in survivors (3).

Balance training and strengthening exercise with resistance for 8 weeks showed improvement in the physical functioning performance, dynamic balance, and fatigue in prostate cancer patients (8). Also, proposed a mixed exercise including aerobic, strength, and sensorimotor training improves the patient’s quality of life, balance control, physical performance, mobility and reduces symptoms of CIPN in lymphoma patients (9).

Few studies have been done to investigate the potentially beneficial effects of specific exercises to counteract the CIPN symptoms in breast cancer patients. Balance training programs specifically developed for CIPN patients are lacking (7).

Thus, the present study aimed to provide an evidence base about the effect of balance training on functional activities and symptoms of CIPN in breast cancer patients. It was hypothesized that balance training would have effects on functional activities and symptoms of CIPN in breast cancer patients.

II. MATERIAL AND METHODS

Study design
It was a randomized controlled clinical trial. The study was approved by the Faculty of Physical Therapy Ethical Committee (NO:P.T.REC/012/002070). Patients were instructed about the study's goals and procedures. A written consent was signed by each participant at starting of the study. The duration of this study was from February/2019 to February/2021.

Sample size calculation was performed using G*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany). It showed that the required sample size for this study was 20 subjects per group. Calculations were made using α=0.05, β=0.2, effect size=0.82, and allocation ratio N2/N1 =1 from a pilot study on 5 subjects.

Subjects
Oncologists referred forty-three breast cancer patients suffering from CIPN. Forty patients met the following inclusion criteria. They received neurotoxic potential chemotherapy including paclitaxel and docetaxel for at least 4 cycles within the previous 6 months as an adjuvant therapy. They reported at least one neuropathic symptom on the chemotherapy induced peripheral neuropathy assessment tool (CIPNAT) (10). In addition, their functional reach test was less than 11.5 inches (30 cm) indicating increased the risk of falling (11). Their age ranged between 40-50 years old and their body mass index (BMI) was >24.9 and <35 Kg/m².

Breast cancer patients were excluded from this study if they had respiratory or heart problems, marked skeletal deformity or bone metastasis, visual system affection, cognition problems, or previous surgeries at their back and lower limbs. Also, if they had any other chronic neuropathic disease including diabetic neuropathy, multiple sclerosis, neuritis, vitamin B deficiency or cervical and lumbar radiculopathy.
Patients were randomly distributed into two equal groups using the closed envelope method. Both control and study groups continued to receive their prescribed chemotherapy dose including paclitaxel and docetaxel. Also, the study group received a selected balance training program for 50-60 min, 2 times/week for 12 weeks.

Assessment

1-Assessment of balance

Functional reach test was used to determine the patients who are at risk of falls. Also, it was used to assess balance for each patient in the control and study groups at starting and after 12 weeks of the treatment course. It is a single valid and reliable item test developed as a quick screen for balance problems and a predictor of fall in older adults (12) and (13). A yardstick was fixed on the wall by adhesive straps. The patient was asked to stand next to, but not touch the wall or the yardstick. She was asked to flex her shoulder to 90 degrees with a closed fist. The examiner stood in front of the patient and recorded the initial reading on the yardstick, usually spotting the knuckle of the third metacarpal. Then, the patient was asked to reach forward with her closed fist as far as she could without taking a step. The location of the end position of the 3rd metacarpal is also recorded. The reach distance was calculated by subtracting the initial reading score from the end position score and recorded in cm. Three trials were performed by each patient. Then, the examiner recorded the average of the last two trials (11).

2- Assessment of neuropathy symptoms and functional activities:

Chemotherapy induced peripheral neuropathy assessment tool (CIPNAT) was used to assess neuropathy symptoms and its interference on the functional activities. It was assessed for each patient in the control and study groups at starting and after 12 weeks of the treatment course. It is composed of the symptom items score that evaluates the neuropathic symptoms, as well as the interference items score that evaluates the functional status and daily challenges. This questionnaire showed a high reliability and validity as a comprehensive assessment of peripheral neuropathy in cancer patients (14).

To calculate the symptom items score, each patient was asked to answer about the occurrence of symptoms (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 severity, distress, and frequency for each symptom using a numeric rating scale of 0 to 10. By adding the range of occurrence (0-9) to the range of 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 (15). 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 (15).

Balance training program.

The selected balance training program was described according to the American cancer society guidelines (16). Balance exercise with strength training play an effective role in improving stability indicis (17). The program started with 5- minute warming up exercises and ended with 5-minute cooling down exercises in the form of march in place. The selected program included stretching, active free, strengthening, and balance exercises. Stretching exercises for pectorals, hamstring, hip flexors, and calf muscles were performed. Active free exercises were practiced for the upper and lower limbs for the first 2 weeks and active resisted exercise for the remaining weeks using dumbbells and sandbags (1 kg). Each exercise was performed 10 repetitions for 2 sets with holding each contraction for at least 6 seconds. Balancing exercises were performed with patients’ eyes opened in the first 2 weeks and closed in the remaining weeks. Exercises included standing on one foot, sit to stand exercise, heel-to-toe walking, pushing in different directions with different standing positions including stride, one-foot step forward and one footstep backward, rocking exercise on balance board, reach forward exercise, and walking in the figure of” 8”. Each exercise was done for 10-15 repetitions. The program lasted for 50-60 minutes, 2 times/week for 12 weeks.

IIII. DATA ANALYSIS:

Descriptive statistics and unpaired t-test were conducted for comparison of subject characteristics between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene’s test for homogeneity of variances was conducted to ensure the homogeneity between group. Mixed MANOVA was conducted to compare the effect of time (pre versus post) and the effect of treatment (between groups), as well as the
interaction between time and treatment. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparison. 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).

IV. RESULTS:

Subject characteristics:
Table 1 showed the subject characteristics of the control and study groups. There was no significant difference between groups in age (p=0.91), weight (p=0.89), height (p=0.54), BMI (p=0.60), and number of chemotherapy cycles (p=0.86).

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

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Mean ± SD Control group</th>
<th>Mean ± SD Study group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>46.30±2.69</td>
<td>46.20±3.17</td>
<td>0.91</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>84.20±7.33</td>
<td>84.60±10.53</td>
<td>0.89</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.30±7.66</td>
<td>163.75±8.29</td>
<td>0.54</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.84±2.78</td>
<td>31.33±3.18</td>
<td>0.60</td>
</tr>
<tr>
<td>Number of chemotherapy cycles</td>
<td>5.10±0.91</td>
<td>5.15±0.87</td>
<td>0.86</td>
</tr>
</tbody>
</table>

SD, standard deviation; p value, probability value

Mixed MANOVA revealed that there was a significant interaction of treatment and time (F(6,33) = 26.01, p = 0.001). There was a significant main effect of time (F(6,33) = 18.86, p = 0.001). There was a significant main effect of treatment (F(6,33) = 9.94, p = 0.001).

As presented in table (2), there was no significance difference in the functional reach distance (p=0.23) and interference items score (p=0.31), while there was a significant increase in the symptom experience items score (p=0.03) in the control group post-treatment. Also, there was a significant increase in the functional reach distance (p=0.0001) and a significant decrease (p=0.0001) in the symptom experience items score and interference items score in the study group post-treatment.

There was no significant difference in the functional reach distance (p=0.58), symptom experience items score (p=0.47), and interference items score (p=0.56) between groups pre-treatment. However, there was a significant increase in the functional reach distance (p=0.0001) and a significant decrease in the symptom experience items score (p=0.0001) and the interference items score (p=0.0001) of the study group compared with those of the control group (table 2).

Table (2): Mean functional reach distance and CIPNAT pre and post treatment of the control and study groups:

<table>
<thead>
<tr>
<th>Pre-treatment</th>
<th>Post-treatment</th>
<th>MD (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Functional reach distance (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td>26.35±1.72</td>
<td>25.75±2.29</td>
<td>0.60 (-0.4:1.6)</td>
</tr>
<tr>
<td>Study group</td>
<td>26.05±1.70</td>
<td>33.50±2.64</td>
<td>-7.45 (-8.45: -6.44)</td>
</tr>
<tr>
<td>MD (95% CI)</td>
<td>0.30 (-0.79; 1.39)</td>
<td>-7.75 (-9.33:-6.16)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>p = 0.58</td>
<td>p = 0.0001</td>
<td></td>
</tr>
<tr>
<td>Symptom experience items score</td>
<td></td>
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</tr>
</tbody>
</table>

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Chemotherapy-induced peripheral neuropathy (CIPN) is a clinically relevant side effect of chemotherapy and a persistent complication of cancer survivors (18). The symptoms of CIPN limits patient’s everyday life activities (19), affects postural stability (20), decreases quality of life (QoL), and increases the risk of falling and fall-related injuries. All these complications result in increasing the risk of mortality (21).

The present study aimed to evaluate the effect of a balance training program on balance and symptoms of CIPN in breast cancer women. The results of this study revealed a significant increase in the functional reach distance, as well as a significant decrease in the symptom experience items score, and interference items score of the study group compared with the control group.

The results agreed with the previous studies, which concluded that exercise intervention was successful in attenuating symptoms of CIPN and improving the overall quality of life (QOL) of breast cancer patients compared to sedentary counterparts (22). A previous review reported that aerobic exercise may be a key component of exercise interventions for CIPN in mixed cancer types and stages, chemotherapy regimens and status, and CIPN presence and severity (23) (Kanzawa-Lee et al., 2020). Also, (24) Tofthagen et al., 2014 reported that the balance training has the highest effect on motor and sensory symptoms on all types of peripheral neuropathies. Another study found that proprioceptive training for 3 weeks can significantly decrease the neuropathic symptoms and improve balance, as well as functional reach distance in CIPN patients (25).

Exercises for 36 weeks, especially sensorimotor training, was a promising method to improve patient’s quality of life, reduce peripheral neuropathy symptoms, and improves patients' balance control, physical performance level, and mobility (9). In addition, (26) Brayall et al., (2018) demonstrated that balance training, strength and endurance training are beneficial for patients with CIPN. These exercises improved static and dynamic balance, increased lower extremity strength, and reduced the symptoms of CIPN such as pain and paresthesia.

Exercise has many beneficial effects on CIPN symptoms. It reduces chronic inflammation, and changes how sensations from the hands, feet, and rest of the body are processed by the brain (27). It induces changes in the brain that counteract central sensitization associated with neuropathic pain, thus may alleviate CIPN symptoms (6). Balance training is known to improve muscular output and induce neuronal adaptations leading to an improvement in postural control (28). Also, (29) Kneis et al., and (30) Dhawan et al., (2020) reported that combined balance and endurance training improved the patients' functional activities, and cardiorespiratory fitness, as well as reduced the pain and sensory symptoms of CIPN. The knee extensor and hip abductor muscles are important for transferring, standing up from a chair, and walking, which are essential for the daily living activities (31). So that increased strength of these muscles could explain a significant decrease in the interference items score, which indicated an improvement of the functional activities in breast cancer women.

The selected program of the present study is a simple, safe and easily applicable. It can be easily performed by breast cancer patients at home. However, this study is limited by that the strength of the lower extremities is not measured that may explain the findings of the study. Further studies are needed to determine the effect of balance training and strengthening exercises on the fatigue, quality of life, and muscle strength in cancer patients with
CIPN. Further research is required to compare between the effect of different types of strengthening exercises including eccentric, isotonic, and isometric on balance control in cancer patients.

VI. CONCLUSION

It can be concluded that balance training should be a part of life in breast cancer women suffering from CIPN to decrease CIPN symptoms, improve balance, and functional activities.

REFERENCES:


