Response of Hand Grip Strength to Task-oriented Training Program in Breast Cancer Patients with Taxanes-induced Peripheral Neuropathy

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ABSTRACT

Background: *A significant fraction of patients undergoing chemotherapy specially Taxanes suffer from peripheral neuropathy affecting hand strength. Task-oriented training, a form of exercise structured as tasks, focuses on improving specific functional abilities through practical, goal-directed activities.* ***Purpose:*** *To evaluate the therapeutic benefits of task-oriented training in improving hand grip strength in patients with taxanes-induced peripheral neuropathy.*

Subjects and methods: *This randomized, single-blind controlled trial included forty-eight female breast cancer patients, aged 35-65, with taxane-induced peripheral neuropathy. They were randomly divided into two groups of 24 each. Over four weeks, with a frequency of three sessions per week, group A (the control group) received traditional physical therapy, while group B (the task-oriented training group) underwent task-oriented training in addition to traditional physical therapy. Hand grip strength was measured using the Takei Analog Hand Grip Strength Dynamometer before and after the four-week intervention.* ***Results:*** *After the 4th week of intervention, the two groups revealed decrease in mean percent change regarding grip strength within each group as a treatment effect. However, when we compared between the two groups regarding these values the two groups were similar.* ***Conclusion:*** *Neither task-oriented training nor conventional physical therapy has a significant impact on hand grip strength in breast cancer patients with taxane-induced peripheral neuropathy. However, patients undergoing task-oriented training may experience delayed onset or less severe symptoms of chemotherapy-induced peripheral neuropathy (CIPN). Hand grip strength decreased in both groups following treatment, with a reduction of 19.5% in the control group and 11.5% in the task-oriented training group, indicating that the task-oriented program potentially delay the onset of CIPN symptoms.*

Keywords: *Hand grip strength; Task-oriented training; Taxanes-induced peripheral neuropathy.*

INTRODUCTION

Breast cancer is the most frequent disease in women worldwide, and for a long time, it was very difficult to cure, which resulted in high rates of morbidity and mortality. The survival rate has increased as a result of recent developments in its diagnosis and treatment. The overall rate of cancer-related deaths among women dropped by 12.3% between 1991 and 2006. Sixty percent of the decrease were related to decreasing the rates of colorectal and breast cancer (1). Chemotherapy is a common and effective treatment option for cancer patients because of its demonstrated ability to increase survival rates. Nevertheless, certain chemotherapy drugs, such taxanes, which are often used to treat breast cancer, may have extremely harmful neurotoxic side effects, which can destroy neural structures through glial damage, inflammation, mitochondrial malfunction, and other processes (2). Taxanes (e.g. paclitaxel, docetaxel) are frequently used in palliative care for patients with advanced disease, neoadjuvant therapy for patients with locally progressed disease, and adjuvant therapy for patients with early-stage cancer. One prevalent side effect of taxanes is chemotherapy-induced peripheral neuropathy (CIPN), which has been shown to have a detrimental effect on patients' quality of life and even clinical results. CIPN affects between 60% and 70% of patients on taxanes, and it's now one of the primary causes of treatment termination at an early stage. The first two months are usually when symptoms of taxane-related neuropathy appear; they then get worse during treatment and sometimes even get worse after treatment is stopped. Because more people are surviving breast cancer thanks to advancements in anticancer therapies, taxanes-induced peripheral neuropathy has emerged as a side effect of treatment (3). The primary signs and symptoms of CIPN include sensory neuropathy, which includes pain, numbness, dysesthesia, hypoesthesia, and hyperesthesia in the distal regions of the upper and lower extremities. Motor neuropathy, which includes weakness and cramping in the muscles, can also occasionally manifest. In relation to the upper extremities, a number of tasks that call for strength in a variety of everyday situations—such as self-care (dressing), household chores (cooking), hobbies, employment, and leisure—become challenging due to the onset or worsening of symptoms in the fingers. Furthermore, some symptoms could not go away for up to two years after the completion of treatment (4).

Many researchers have highlighted the benefits of physical activity in mitigating chemotherapy-induced peripheral neuropathy (CIPN). A systematic study discovered that exercise conducted peri chemotherapy lowers CIPN symptoms and neuropathic pain, and exercise performed during a range of chemotherapy regimens improves CIPN symptoms and postural control. Exercise has also been demonstrated to health-related quality of life (HR-QoL) during chemotherapy, and to decrease fatigue and quality of life specific to the disease site during adjuvant treatment for breast cancer. This occurs through controlling the expression of the anti-inflammatory cytokines IL-10 and IL-1RA, brain-derived neurotrophic factor (BDNF), insulin-like growth factor 1 (IGF-1), and other factors. This may point to a mechanism for reducing nerve damage and/or attenuating inflammation, which has been linked to the genesis of CIPN and its symptoms. Exercise can boost mitochondria's electron transport chain efficiency and antioxidant capacity, and preclinical research has demonstrated that acute exercise enhances the capacity of mitochondria to store Ca2+ prior to mitochondrial permeability transition pores

(MPTP) opening (5). Task-oriented exercise aims to increase performance in a functional task by goal-directed practice and repetition, and it is significantly benefiting the patient. Evidence suggested that learning particular skills maximizes the improvements in neural plasticity (6).

MATERIALS AND METHODS

Study design:

The study was single blind (participants) randomized control trial. Before the beginning of the study, ethical approval was given by The Faculty Physical Therapy's Ethical
Committee (P.T.REC/012/00460).
Institutional Review Board of National Cancer Institute also approved this trial (2307-405-034).

Sample size determination:

Sample size calculation was done using hand strength, as reported in Ikio et al, (2021), with 80% power at $\alpha = 0.05$ level, number of measurements 2, for two groups and effect size = 0.415 using F-test MANOVA within and between interaction effects. The minimum proper sample size is 48 subjects, 24 subjects in each group. The sample size was calculated using the G*Power software (version 3.0.10) (4).

Participants:

Patients were recruited from the National Cancer Institute and assessed for eligibility based on specific criteria. Only those aged 35-65 years with taxane-induced peripheral neuropathy affecting the upper limbs were included. Exclusion criteria comprised pain or numbness in the upper extremity from other causes (e.g., trauma, CNS diseases such as cerebral infarction), other neurological conditions (e.g., diabetes, rheumatoid arthritis, cervical myelopathy), bone, brain, or spinal cord metastases, a history of psychiatric disorders (e.g., depression, schizophrenia), cognitive decline preventing active participation, or cases of acute neuropathy like that caused by oxaliplatin. Forty-eight patients participated in this trial after being informed about its nature, objectives, and potential benefits, and they provided written consent. They were randomly assigned to one of two equally sized groups; control group and task-oriented training group. The random assignment was conducted using sealed envelopes containing name cards, with participants allocated to groups based on the card drawn. The treatment commenced one week after the randomization process.

Interventions:

Patients in both groups underwent identical conventional therapy for chemotherapy-induced neuropathy over a 4-week period, with sessions occurring three times per week. This therapy consisted of mobilization exercises targeting the wrist, metacarpophalangeal joints (MPJ), and interphalangeal joints to enhance or preserve range of motion. Additionally, strengthening exercises using a gel ball or Thera-band were employed to strengthen muscles in the hands and wrists, alongside stretching exercises (4). In addition to conventional therapy, patients in the task-oriented training group participated in a program involving specific tasks, including; 1. Instructing the patient to place their hand flat on the table and rapidly tap each finger twice; 2. Having the patient hold a pen and draw circles on a sheet without allowing their hand or arm to touch the paper; 3. Tasking the patient to hold 10 coins in their palm and slide them one by one onto the table using their index finger and thumb, while keeping the remaining coins in their palm; 4. Asking the patient to quickly turn 10 differently sized coins placed on defined spots; 5. Having the patient turn nuts and screws as quickly as

possible; 6. Instructing the patient to mold clay into a ball and flatten it with the palm of their hand; 7. Asking the patient to create a roll using clay, make notches on its lateral side with their hand, and then move their fingers over these notches while keeping their hand flat on the table, repeating this process five times; 8. Tasking the patient with creating a chain of paper clips and then unfastening them (7,8).

Outcome measures:

The assessment of outcome measures took place at two specific time points: initially, and at the conclusion of the four-week post-intervention period. The primary outcome measure was conducted using a hand dynamometer, which was utilized to quantify hand grip strength. The patients were positioned sitting upright in a chair, with their knees and hips at 90° flexion and with back support. The shoulder was adducted against the body, the elbow positioned in 90° flexion (unsupported) and the wrist in a neutral position. The patients were asked to squeeze the handle with maximal effort for at least 5 seconds and were given verbal encouragement. Both hands were tested three times with maximal effort, and average HGS values were mainly recorded and analysed. HGS values were measured in kilograms (9,10).

Data analysis

The Statistical Package for the Social Sciences (SPSS) from Chicago, Illinois, USA (version 28) was used to analyze the data. All reported data were given descriptive summaries. The mean and standard deviation were used to display continuous data. Representations of frequencies and percentages were used to illustrate categorical data. The relationship between the qualitative variables was examined where suitable using the chi-square (Fisher's exact) test. The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine whether the data were normal; the results showed that the data were not normally distributed, Thus, The Wilcoxon signed rank test was utilized to compare values of physical therapy outcome at baseline from values after physical treatment, however the Mann Whitney U test was applied to compare two groups regarding numerical variables at base line and then after physical treatment. An investigation of Spearman's rho correlation was conducted. In order to distinguish between grade 2 and grade 3 neuropathy, the best cut-off dose values per cycle were estimated using a receiver operating characteristics (ROC) curve analysis. Additionally, the diagnostic accuracy was estimated by calculating the sensitivity, specificity, positive predictive value, negative predictive value, and total accuracy along with their 95% confidence interval. All tests were two-sided, and a p-value of < 0.05 was considered statistically significant.

RESULTS

- Subjects' characteristics:

Table (1) shows the characteristics of the studied patients in both groups which revealed that there was no significant difference between groups in age, weight, height, BMI ($p > 0.05$).

Table 1. Comparison of characteristics of the studied patients in both groups

	Control group	Task-oriented training group	p value
	Mean ±SD	Mean ±SD	
Age (years)	54.0 (35.0-65.0)	50.5 (35.0-67.0)	0.529
Weight (kg)	77.5 (59.0-117.0)	79.5 (49.0-108.0)	0.690
Height (cm)	159.0 (145.0-173.0	159.5 (144.0-172.0	0.773
BMI (kg/m^2)	30.8 (22.2-47.5)	31.2 (21.8-40.6)	0.652

SD, Standard deviation; MD, Mean difference; p value, Probability value.

- Within group comparison:

Following treatment, hand grip strength (HGS) had decreased in both groups. in The control group, the HGS percentage was - 19.5%. while in the task-oriented training group, the percentage was - 11.5%. and despite this decrease, Table (2).

- Between group comparison:

Following treatment, we found a non-significant difference between the two groups (p-value between groups= 0.160), Table (2).

Table 2. Mean Hand grip strength pre and post treatment of both groups:

	Control group	**Task-oriented training group**		
	Mean ±SD	**Mean ±SD**	**MD**	**p value**
Pre treatment	8.1 (4.1-12.5)	7.3 (3.0-11.4)	0.8	0.712
Post treatment	6.5 (1.5-10.0)	6.3 (3.3-11.7)	0.2	0.912
MD	- 1.6	- 1		
% of change	- 19.5%	- 11.5%		
p-value within groups (Wilcoxon signed rank test)	<0.001	0.002		

SD, Standard deviation; MD, Mean difference; p value, Probability value

DISCUSSION

One in every eight women will develop breast cancer in their lifetime, making it the most common malignant tumor in women. Compared to other CIPN kinds, Taxanes induced peripheral neuropathy (TIPN) is very common and has unique pathophysiologic processes, onset, and symptom patterns. TIPN symptoms usually appear within the first two months of treatment, get worse throughout it, and can persist after it ends, which might lead to treatment ceasing (11). One of those impairments is decreased hand grip strength after chemotherapy (12). The combination of sensory abnormalities and reduced skilled hand function is a hallmark of motor abnormalities in people with CIPN (13). According to research findings, task-oriented training can improve functional movement in rehabilitation settings, enabling the effective performance of musculoskeletal and neuromuscular systems within natural environments (14).

This study was conducted to investigate the response of hand grip strength to task-oriented training program (TOT) in breast cancer patients with taxanes induced peripheral neuropathy (TIPN). To our knowledge, no research has specifically investigated the response of TOT hand grip strength in patients with taxanes induced peripheral neuropathy. Our trial outcomes are consistent with two previous studies, which have demonstrated that hand exercises have limited effect on TIPN motor symptoms (15,16), our data provides preliminary evidence that women who

engage in task-oriented training program during taxane chemotherapy for breast cancer may have delayed onset or less severe TIPN motor symptoms.

Bland (2017) studied the impact of exercise on taxane side effects in 24 women with early-stage breast cancer. Participants were randomized to either a thrice-weekly exercise group (EX) (n=11) or a usual care group (UC) (n=13) during taxane chemotherapy (4 cycles, 2-3 weeks apart). Patient-reported CIPN symptoms were measured at baseline (pre-chemotherapy), 0-3 days before the fourth chemotherapy cycle, and at the end of chemotherapy, using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ) to assess motor and sensory CIPN symptoms. The study found a significant main effect of time on the motor symptom subscale (p=0.04). Mean motor symptoms increased significantly from baseline to the end of chemotherapy in both groups (from 6.3±2.2 to 16.5±3.2, p=0.01), with no significant differences between the groups at any time point. Maximal handgrip strength showed no significant differences. Overall, motor symptoms worsened over time in both groups, peaking at the end of chemotherapy. Although mean motor symptom scores were higher in the usual care group compared to the exercise group, indicating worse CIPN, this difference was not statistically significant (15).

Wu et al. (2022) conducted a pilot study involving 13 breast cancer survivors experiencing chemotherapy-induced peripheral neuropathy (CIPN) from a hospital in northern Taiwan. This study employed a single group with repeated measures and a quasi-experimental design. The intervention was a four-week, home-based extremity exercise program, consisting of 10 skilled hand exercises and Buerger-Allen exercises. The objective severity of CIPN was assessed using the Total Neuropathy Score clinical version (TNSc) before the exercise program (T1), during the program (T2 to T4), and after the program (T5). The TNSc scores increased from T1 to T2, peaked at T2, then decreased from T3 to T4, reaching the lowest score at T5. Although the outcome measure was insignificant for clinician-assessed CIPN, it was significant for patient-reported CIPN after the intervention (16).

On the other hand, Ikio et al. (2021) examined the effect of combined hand exercises in 42 CIPN patients who were randomly assigned to either the intervention (n=21) or control (n=21) groups. Participants were evaluated at baseline (T0), after one chemotherapy cycle (T1), and after two chemotherapy cycles (T2). Muscle strength was evaluated as grip and pinch strength (pulp pinch), which was measured using a digital hand dynamometer (T.K.K.5401, Takei Kiki Kogyo) and a digital pinch gauge (JAMAR Plus+ Digital Pinch Gauge). Both evaluations were performed with the dominant hand, and the maximum value of the two measurements was adopted at the end. They found that performing a combined hand exercise intervention may prevent worsening in the activities of daily living using upper extremities in patients with chemotherapy-induced peripheral neuropathy (4).

From my point of view, despite a decrease in hand grip strength (HGS) in both groups, the task-oriented training program demonstrated a slower rate of decline (-11.5%) compared to the control group (-19.5%), indicating that it was more effective in delaying the progression of chemotherapy-induced peripheral neuropathy (CIPN). This slower rate of decline suggests that task-oriented training better preserved muscle functionality and

coordination essential for daily activities. The program's focus on functional tasks likely provided greater neuromuscular benefits, mitigated some of the negative impacts of CIPN, and delayed the onset of severe symptoms. Furthermore, the task-oriented training might have promoted physiological adaptations such as improved neural function, microcirculation, and neuroplasticity, which contribute to maintaining nerve health and delaying CIPN progression. Overall, patients in the task-oriented group likely experienced better quality of life and functional capacity, despite the decrease in HGS, making this intervention more effective than conventional physical therapy in managing CIPN.

The study has certain limitations. Firstly, it did not consider additional factors that could potentially influence hand grip strength and CIPN, such as patient activity level, and comorbidities. Therefore, further research is needed to address these factors adequately. Secondly, the cumulative effects of chemotherapy likely played a key role in the reduced general muscle strength observed. Furthermore, the study's statistical analysis was limited by the lack of long-term follow-up data, which is crucial for evaluating the treatment's lasting benefits and understanding the prolonged impact of chemotherapy on muscle strength. Consequently, additional research is necessary to assess the long-term effectiveness of the task-oriented training program in managing CIPN and preserving hand grip strength in breast cancer patients undergoing taxane chemotherapy.

CONCLUSION

Based on the findings of this study, no significant differences were observed in the means before and after interventions in both groups. However, our data suggests that women who participate in a task-oriented training program during taxane chemotherapy for breast cancer may experience a delayed onset or less severe CIPN symptoms and this decline in hand grip strength is likely affected by the cumulative impact of chemotherapy, which generally reduces overall muscle strength.

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Conflict of interest

There was no disclosure of any potential conflicts of interest related to this article.

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