

EFFECT OF EXERCISE IN MANAGEMENT OF CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY: EVIDENCE –BASED REVIEW.



Nour Ali Alrida<sup>1</sup>, Amal Mohammad Taysier Ababneh<sup>2</sup>, Yasmeen Abu Sumaqa<sup>3</sup>

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**Abstract**

Background: Chemotherapy-induced peripheral neuropathy is a significant, debilitating symptom directly related to the administration of neurotoxin chemotherapy for cancer treatment. Effective management for chemotherapy-induced peripheral neuropathy is lacking and therefore treatment options are limited. Exercise has been shown to counteract disease and treatment-associated side effects and considers an effective supportive therapy method Purpose: the purpose of this manuscript was to map and summarize the findings of the current research studies that discuss the effectiveness of exercise in the management of chemotherapy-induced peripheral neuropathy among cancer patients. Methodology: CINAHL, Google Search, and PubMed were used. Only seven studies met the inclusion criteria. All included studies were appraises for the level of evidence. Findings: the results of the included articles showed that exercise programs can reduce symptoms of chemotherapy-induced peripheral neuropathy among patients with cancer.

**Keywords:** chemotherapy-induced peripheral neuropathy, CIPN, management, exercise, physical activity

<sup>1</sup>RN, MSN, Full-time lecturer, Applied Science Department/Ajloun College, Al-Balqa Applied University, P.O. 206, Al-Salt, Jordan.

<sup>2</sup>RN, MSN, School of Nursing, Jerash University, P.O. 26150, Jerash – Jordan

<sup>3</sup>RN, PhD, Assistant Professor, Faculty of Nursing, Zarqa University, P.O. 2000, Al-Zarqa –Jordan  
Email: nour.ali@bau.edu.jo,amal.ababneh@jpu.edu.jo,yabusumaqa@zu.edu.jo

**Introduction**

Nursing as a profession develops and continues to be ranked the most trusted profession, with the highest honesty and ethical standards according to the annual Gallup poll ranking of honesty and ethics in various fields (American Nursing Society, 2017). To improve nursing practice, improve health delivery, and patient and health system outcomes, the professional nursing practice should be evolved need to research utilization to evidence-based practice (Fink, Thompson & Bonnes, 2005). The objective of the current paper is to translate science derived from research articles to practice. Chemotherapy-induced peripheral neuropathy is a widely common serious and dose-limiting side effect of cancer treatment (Cavaletti & Marmiroli, 2010). Especially with those patients who receive platinum analogs, antitubulins (eg, taxanes and vinca alkaloids), bortezomib, and thalidomide (Quasthoff &

Hartung, 2002). Chemotherapy-induced peripheral neuropathy would develop among 10-100% of patients who received chemotherapy (Oncology Nursing Society, 2018). The sensory symptoms of chemotherapy-induced peripheral neuropathy could present in the feet and/ or hands (stocking, gloves pattern); pain, numbness, or tingling, manifested as weakness, cranial nerve deficits, or autonomic neuropathy (Miltenburg & Boogerd, 2014). Chemotherapy-induced peripheral neuropathy can persist from months to years after chemotherapy completion, which will cause significant challenges for cancer survivors due to its negative impact on functional abilities and quality of life (Bakitas, 2007). Effective management for chemotherapy-induced peripheral neuropathy is lacking and therefore

treatment options are limited (Addington & Freimer, 2016).

Exercise is a physical activity performed to improve or maintain one or more of the components of physical fitness: cardiorespiratory endurance (aerobic fitness), muscular strength, muscular endurance, flexibility, and body composition (Porcari, Bryant & Comana, 2015). Exercise intervention in a patient with cancer has been provided as home-based, patient self-managed programs, and supervised and unsupervised individual or group exercise sessions (Mohammad et al. 2022; Oncology Nursing Society, 2018). Exercise has been proven to counteract disease and treatment-associated side effects (e.g., Fatigue and lymphedema), and considers an effective supportive therapy method (Kessels, Husson & van der Feltz- Cornelis, 2018; Baumann et al., 2018). There is emerging evidence that exercise can modify or prevent peripheral neuropathy induced by diabetes mellitus (Balducci et al., 2006). Also, improvement in neuropathic symptoms and cutaneous nerve fiber branches had been proved following supervised exercise in people with diabetic peripheral neuropathy (Kluding et al., 2012). Resistance exercise training improves and increases lower limb (especially knee and ankle) speed of strength generation among patients with diabetic peripheral neuropathy (Handsaker, Brown, Bowling, Maganaris, Boulton & Reeves, 2016). Therefore, this review aimed to investigate and summarize the findings of the current research studies that discuss the effectiveness of exercise in the management of chemotherapy-induced peripheral neuropathy among cancer patients. Also, to answer PICO question “Is exercise program manage chemotherapy induce peripheral neuropathy?”

### Significance

The severity of chemotherapy-induced peripheral neuropathy range from some loss of sensory function and mild paresthesia to neuropathic pain (Scripture, Figg & Sparreboom, 2006). As a matter of fact, the health impacts related to chemotherapy-induced peripheral neuropathy remain worrying; because chemotherapy-induced peripheral neuropathy is associated with comorbidities such as psychological distress, fall risk, and sleep disorders (Hong, Tian & Wu, 2014; Winters-Stone et al., 2017; Alhusban, 2019; Shosha et al., 2013), a decline in physical functioning and increased risk of depression in older cancer survivors (Ababneh, 2018; Leach, Bellizzi, Hurria & Reeve, 2016). Symptoms of

chemotherapy-induced peripheral neuropathy have affected the ability to work among breast cancer survivors (Alhusban et al., 2019; Zanville et al., 2016). Chemotherapy-induced peripheral neuropathy represents a heavy economic burden on the health system in the country. For example, in the USA, on average chemotherapy induce peripheral neuropathies increase healthcare costs by \$17,344 per year per patient (\$36,660 for head and neck cancer, \$18,790 for non-small cell lung cancer, \$16,940 for breast cancer, and \$5,140 for ovarian cancer) (Pike, Birnbaum, Muehlenbein, Pohl & Natale, 2012). Exercise training was associated with significant improvements in muscular strength, aerobic capacity, functional quality of life, fatigue, anxiety, and self-esteem (Speck, Courneya, Mâsse, Duval & Schmitz, 2010). In addition, exercise training is a beneficial supportive therapy both during and after the completion of adjuvant therapy in adult cancer patients, with a low incidence of adverse effects (Jones & Alfano, 2012). This review will recognize and estimate the evidence of exercise effect in managing chemotherapy induce peripheral neuropathy among cancer patients.

### The PICO Summary

Population (P): the population of the current review is patients with cancer who have chemotherapy-induced peripheral neuropathy.

Intervention (I): the intervention is Exercise.

Comparison (C): the comparison is between the intervention group doing exercise and the control group not doing any intervention but just receiving usual care.

Outcome (O): the outcome is to manage chemotherapy induce peripheral neuropathy.

### PICO question.

Is the exercise program manage chemotherapy induce peripheral neuropathy?

### Methodology

A comprehensive literature search was conducted in March 2019 to look for articles related to the main topic “Effect of Exercise in Management of Chemotherapy Induced Peripheral Neuropathy”. The search was conducted using the electrical databases of CINAHL, Google Search, and PubMed.

The keywords used to find the articles were: chemotherapy-induced peripheral neuropathy, CIPN, management, exercise, and physical activity. These keywords were used as consistent terminology among searched

databases. The inclusion criteria for this evidence-based review were the following: (1) They encompassed information about the use of exercise in managing chemotherapy-induced peripheral neuropathy; (2) The articles were written in the English language; (3) They were published between 2014 and 2019; (4) Full-text articles.

About 130 articles have resulted from the searched literature. And after excluding not related studies (108 articles); duplicate articles (6); not full text (3); not management study (5); animal studies (2); the total number of articles was reduced to seven articles according to the previously described inclusion criteria.

### Methodological and Sample Characteristics

The majority of the obtained articles for this review were randomized controlled trials, all of them discussed exercise as an intervention to manage chemotherapy-induced peripheral neuropathy. Different types of valid and reliable

questionnaires and tools were used to obtain data about the effect of exercise on chemotherapy-induced peripheral neuropathy.

The sample sizes of the included articles ranged from 20 to 2154 adult patients with cancer, the majority of participants were females. The evidence level of the included articles was assessed according to Evidence-based nursing care guidelines (Ackley, Swan, Ladwing & Tucker, 2008), (Appendix A). However, the assessed level of evidence in the majority of the included articles was high. Where one study was a highly strong level of evidence (level I) systematic review (Duregon et al., 2018), four studies with a strong level of evidence (level II) randomized control trial (Schwenk et al., 2016; Kleckner et al., 2016; Zimmer et al., 2017; Kleckner et al., 2018; Kavitha & Vaidya Nathan, 2017), and one study with a low level of evidence (level IV) prospective cohort study (Mols et al., 2015).

#### Appendix A

Level of evidence (LOE)	Description
Level I	Evidence from a systematic review or meta-analysis of all relevant RCTs (randomized controlled trial) or evidence-based clinical practice guidelines based on systematic reviews of RCTs or three or more RCTs of good quality that have similar results.
Level II	Evidence obtained from at least one well-designed RCT (e.g. large multi-site RCT).
Level III	Evidence was obtained from well-designed controlled trials without randomization (i.e. quasi-experimental).
Level IV	Evidence from well-designed case-control or cohort studies.
Level V	Evidence from systematic reviews of descriptive and qualitative studies (meta-synthesis).
Level VI	Evidence from a single descriptive or qualitative study.
Level VII	Evidence from the opinion of authorities and/or reports of expert committees.

This level of effectiveness rating scheme is based on the following: Ackley, B. J., Swan, B. A., Ladwig, G., & Tucker, S. (2008). *Evidence-based nursing care guidelines: Medical-surgical interventions*. (p. 7). St. Louis, MO: Mosby Elsevier.

### Findings

Exercise program as an intervention to manage chemotherapy-induced peripheral neuropathy among cancer patients is a feasible and effective method. There was a consensus among the included studies about the effectiveness of exercise in reducing symptoms of chemotherapy-induced peripheral neuropathy. Furthermore, symptoms of chemotherapy-induced peripheral neuropathy among patients with advanced stages could be stabilized by performing an exercise program.

#### Single Modal Exercise Intervention Program

In 2015, Mols and her colleagues conducted a prospective population-based survey, level IV evidence, to gain insight into the association between physical activity, chemotherapy-induced peripheral neuropathy, and health-related quality of life. These researchers used a sample size of 2154 adult colorectal cancer survivors. They used European Organization for Research and Treatment of Cancer Quality of Life Questionnaire and 20- items Chemotherapy Induced Peripheral Neuropathy Questionnaire

(EORTC QLQ- CIPN20) to assess chemotherapy-induced peripheral neuropathy among participants who followed or not followed Dutch Physical Activity Guideline of 150 min of moderate to vigorous aerobic physical activity per week (walking, bicycling, gardening, and housekeeping). They found that following physical activity guidelines of 150 min per week significantly reduced symptoms of chemotherapy-induced peripheral neuropathy (Mols et al., 2015). Moreover, Schwenk and his colleagues (2016) conducted a single-blinded randomized controlled pilot trial, with level II of evidence. To investigate the effect of an interactive motor adaptation balance training program based on wearable sensors for improving balance in older cancer patients with chemotherapy-induced peripheral neuropathy. 22 subjects were randomly assigned to either an intervention or control group. Where subjects in the intervention group received interactive game-based balance training with repetitive weight shifting and virtual obstacle crossing tasks (2 sessions per week (45 min for each session) for 4 weeks). While subjects in the control group continued their normal activity. The results showed that the sway of the hip, ankle, and center of mass was significantly reduced among the intervention group (Schwenk et al., 2016).

### Multimodal Exercise Intervention Program

Kleckner and his colleagues (2016) conducted a nationwide, phase III, randomized controlled trial, with level II of evidence, to examine the effect of exercise on chemotherapy-induced peripheral neuropathy. 314 subjects were randomly assigned into intervention and control groups, where subjects in the intervention group performed standardized, individualized, moderate-intensity, home-based, six-week progressive walking and resistance exercise programs. While the control group received chemotherapy without performing any type of exercise. The results showed that symptoms of chemotherapy-induced peripheral neuropathy (numbness and tingling) among the intervention group were reduced. Furthermore, this reduction was significant among older patients who were allocated to the intervention group (Kleckner et al., 2016).

Similarly, another RCT study with a level of evidence II and a sample size of 355, was conducted by Kleckner and his colleagues (2018). They used the same research methodology, and exercise program and showed the same results exercise reduced symptoms of chemotherapy-induced peripheral neuropathy

more for patients who had breast cancer (Kleckner et al., 2018).

Zimmer and his colleagues (2017) conducted a randomized controlled study, with level II of evidence, to investigate the influence of a supervised exercise program on chemotherapy-induced peripheral neuropathy. These researchers used a sample of 30 patients with metastatic colorectal cancer (stage IV). Subjects were randomly assigned to an intervention or control. The intervention group performed an eight-week supervised exercise program of 60 min (aerobic, resistance, and balanced training) twice per week. Whereas standard recommendations were given to obtain physical fitness. Chemotherapy-induced peripheral neuropathy was assessed using the Functional Assessment of Cancer Therapy/ Gynecologic Oncology Group Neurotoxicity (FACT/GOG-NTX) Questionnaire (German Version 4). The results of this RCT showed that chemotherapy-induced peripheral neuropathy symptoms remained stable among subjects in the intervention group, while the increased intensity of these symptoms was in the control group. As well as, the intervention group showed improvement in the strength and balance function more than those in the control group (Zimmer et al., 2017).

In 2018, Duregon et al. conducted a systematic review, with level I of evidence. This systematic review consisted of five research articles; with sample sizes ranging between 14- 56 subjects. Four of these articles investigated the effect of exercise on chemotherapy-induced peripheral neuropathy symptoms. The results showed that symptoms of chemotherapy-induced peripheral neuropathy were significantly reduced among those participants who performed recommended exercise (Duregon et al., 2018). Finally, Kavitha and her colleagues (2017) conducted a randomized controlled trial, to examine the outcome of a care bundle approach in reducing symptoms of chemotherapy-induced peripheral neuropathy. 20 subjects were randomly allocated into an intervention group and a control group. Subjects in the intervention group performed three care bundle approach for 12 weeks (strength, balance training exercise, massage therapy, and health education session). While the control group received the usual care. The results of this study showed that the care bundle approach reduced symptoms of chemotherapy-induced peripheral neuropathy among the intervention group (Kavitha, Vaidya Nathan & Gopi, 2017).

## Conclusion and Recommendation

Is the exercise program manage chemotherapy-induced peripheral neuropathy? The evidence presented in this manuscript suggests that exercise programs would be a feasible and effective intervention for counteracting and managing chemotherapy-induced peripheral neuropathy among patients with cancer. In addition, standardized, individualized, multimodal exercise programs during and/ or after cancer treatment, with moderate intensity, and for a duration ranging between 30- 120 minutes with a frequency of 2 days per week have proven to be effective in reducing symptoms of chemotherapy-induced peripheral neuropathy among all patients with cancer especially older patient and patients with breast cancer. The researcher recommends that healthcare providers should develop an individualized exercise program with caution to take all safety measures according to the patient's age, cancer type, cancer stage, and health conditions, which may lead to decreased cost-effectiveness of chemotherapy-induced peripheral neuropathy management.

## Conflict of Interest

The author has no conflict of interest to declare.

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## Ethical Approval and Consent to participate

Not applicable.

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