https://menj.journals.ekb.eg
Print ISSN: 2735-3974
Online ISSN: 2735-3982
DOI:

MNJ
Menoufia Nursing Journal
Faculty of Nursing
Menoufia University

Effect of Evidence Based Practice on Chemotherapy Induced Peripheral Neuropathy among Cancer Patients

Asmaa Sobhy Abdelaziz[1], Gehan H. Soliman[2], Seham Mohamed Abd Elalem[3], Shaimaa Adel Mohamed[4], &Amira Hegazy[5]

[1]Assistant lecture Medical Surgical Nursing,
[2,3]Professor of Medical Surgical Nursing,
[4] Lecturer of Medical Surgical Nursing,
[5]Lecturer of clinical oncology and nuclear medicine,
Faculty of medicine, Menoufia university, Egypt
[1,2,3,4]Faculty of Nursing, Menoufia University.

Abstract: Background: Chemotherapy-induced peripheral neuropathy (CIPN) is a Serious adverse event that significantly deteriorates the quality of life and survivorship. **Purpose of the study**: is to evaluate the effect of evidence based practice on chemotherapy induced peripheral neuropathy among patients with cancer. **Design**: A quasi-experimental research design was utilized. **Setting**: The study was conducted at oncology department at Menoufia University Hospital, Menoufia governorate, Egypt. **Sample**: A consecutive sample of 100 adult cancer patients who are receiving chemotherapy were divided randomly and assigned alternatively into two equal groups (study and control) groups. **Instruments**: Three instruments were used in data collection; 1) A Structured Interview Questionnaire, 2) Total Neuropathy Score (TNS), and 3) Observational checklist. **Results**: The results revealed that there was highly significant improve in the total neuropathy score with the end of 12 weeks at follow up with (P= .000**). **Conclusion**: Evidence based practice are powerful in improving the neuropathy symptoms for patients receiving chemotherapy. **Recommendation**: Supervised health teaching program should be carried out for all cancer patients from the beginning of the chemotherapy medication about the importance of exercise and cold therapy to reduce CIPN and a colored booklet should be available and distributed about disease.

Key words*: Chemotherapy induced peripheral neuropathy; Evidence based practice, neuropathy symptoms & cancer patients*

Chemotherapy induced peripheral neuropathy (CIPN) is among the most common long-term adverse effect of many antineoplastic agents, and decreases QOL in cancer survivors with symptoms that include pain in the

hands and feet with associated inability to complete basic activities of daily living (ADLs) and risk of falling. It can be extremely painful and/or disabling, causing significant loss of functional abilities and decreasing quality of life. The incidence of CIPN is related to dose intensity, cumulative dose, co administration of other neurotoxic chemotherapy agents, and pre-existing conditions such as diabetes and alcohol abuse (Gewandter et al., 2021).

Chemotherapy Induced Peripheral Neuropathy is sometimes mild and reversible, whereas in other cases, it can be severe and irreversible, interfering with daily activities. CIPN prevalence depends on the chemotherapeutic agent, dosage, and duration. It was found that 68.1% of patients experience CIPN within the first month after chemotherapy, 60.0% at 3 months, and 30.0% at 6 months and beyond (considered chronic CIPN). It also can develop, or continue to worsen, several months after treatment has stopped, in a phenomenon termed ‘‘coasting’’. Patients can have significant difficulty in essential daily functions including difficulty in fine finger movement such as buttoning clothing, and unsteady gait (numbness, loss of joint position sense); pain on walking (mechanical hypersensitivity); inability to remove items from a fridge, or exacerbation in cold weather (cold hypersensitivity) (Mattar., 2024).

Evidence based practice is considered the basis of nursing practice, which is challenging to implement. However, it can encourage nurses to deepen their understanding of evidence-based nursing, thus improving the quality of nursing work. It is needed to reduce the physical, psychological, and social discomfort experienced from the chemotherapy on the patients (Barnes, 2024).

Non-pharmacological interventions have been proposed to be used in CIPN, mostly as adjuvant to pharmacological treatments. Non-pharmacological interventions have been proposed to be used in Peripheral neuropathy, mostly as adjuvant to pharmacological treatments. The use of complementary medicine and a variety of rehabilitative methods, such as exercise, Acupuncture, Cryotherapy, Compression therapy, Exercise therapy and Ganglioside-monosialic acid. Exercise and cold application, have been tested with positive effects in reducing the impact of CIPN symptoms and in improving the life quality of the patient (Liampas etal., 2021).

Cold therapy has been tested with positive effects in reducing the impact of CIPN symptoms and in improving patient’s quality of life. Knowing the effect of cold application as another non pharmacological method has an important role in the symptom management. The vasoconstriction due to the local effect of the cold slows the cellular metabolism by decreased blood flow. Cold application also reduces the sensitivity of pain receptors (nociceptors) by reducing the release of vasodilator substances. It also decreases the metabolic rate and cellular chemical activity via causing the capillary contraction. It also reduces muscle spasm by decreasing nerve conduction velocity and muscle excitability. The expected effect of cold

application depends on the application period, the temperature used, and the size of the application area. The cold application was reported to reduce the severity of neuropathy (Kunutsor et al., 2024).

The exercise therapy has positive effects in reducing CIPN symptoms in cancer patients. Exercise has been found to treat CIPN symptoms through sensory pathways through the induction of an anti-inflammatory environment with each bout of exercise; by increasing the supply of blood, glucose, and oxygen to mitochondria and, in turn, reducing neuropathic symptoms; and by improving sensorimotor functions for cancer patients with CIPN symptoms (Lin et al., 2021).

Nurses has an important role is managing CIPN as should focus on assessment the patient potential side effects of chemotherapy. Providing specific educational nursing instructions regarding symptoms that need to be reported, educate the patient complementary and integrative guidelines that improving quality of life and help in minimizing patient suffering chemotherapy complications. Nurses must be aware about complementary therapies such as cold therapy exercises teaching patients safe exercise tips for peripheral neuropathy that improve blood and nutrient flow to the legs and feet, reduce swelling, strengthen and stabilize weakened muscles also teach the patent coping and methods of relive fatigue that affect the way of think and feel leading to depression anxious or stress and affects the quality of life and activity of daily living (Abdollahi et al.,2020).

Significance of the Study

Chemotherapy-induced peripheral neuropathy (CIPN) is a major neurologic complication of many chemotherapeutic agents, has a negative impact on patient's quality of life (QoL) and frequently requires dose modification or treatment discontinuation. The incidence of CIPN ranges between 30% to 55% among patients receiving neurotoxic drugs, and approximately 68% of those patients develop CIPN in the first month of treatment (Maihöfner et al., 2021).

Timely recognition of the possible toxicities is influential on the treatment outcome. Since CIPN influences the individual not only physically but also psychologically and socially, the nurse should plan the patient's private intervention by periodic evaluations in the treatment process. There are limited research which study the effect of evidence based practice including exercise and cold application in reducing the impact of CIPN symptoms and in improving the patient quality of life (Dhawan et al., 2020).

Since cold therapy diminished blood flow to the extremities through reducing blood flow to them and as a result reduce the amount of drug flowing through their vessels, limiting the injury to local peripheral nerves. Exercise can help to better manage blood sugar, strength muscles, lower high blood pressure, improve blood flow to the extremities, prevent muscle wasting, reduce cramps and improve sleep better all this benefits will help to manage or reduce neuropathic symptoms (John et al.,2018).

So, it is hoped that the current study opens the door for evidence based practice (cold therapy and exercise) and determine the effect of evidence based practice on chemotherapy induced peripheral neuropathy among cancer patients.

Purpose of the Study

The purpose of the current study is to evaluate the effect of evidence based practice on chemotherapy induced peripheral neuropathy among cancer patients.

Research Hypothesis:

The following research hypotheses are formulated in an attempt to achieve the purpose of the study.

- ❖ Study group patients who are receive evidence based practice may exhibite peripheral neuropathy symptoms lesser than patients who don't (control group).

Research design:

A quasi experimental research design was utilized to achieve the aim of this study.

Setting:

The current study was conducted in the oncology department at Menoufia University Hospital, Menoufia governorate, Egypt.

Subjects:

A consecutive sample of 100 adult cancer patients who were received chemotherapy were divided randomly and assigned alternatively into two equal groups (study and control), 50 patients for each group:

- **Study group (I):** Patients who were received evidence-based practice (cold therapy and exercise) along with routine hospital care.
- **Control group (II)**: Patients who were received routine hospital care only (administration of chemotherapy only).

The study and control group were selected according to inclusion and exclusion criteria:

Inclusion criteria:

- Adult patients with cancer who receive chemotherapy.
- Willing to participate in the study.
- Patient who has chemotherapy induced peripheral neuropathy symptoms.

Exclusion criteria:

- Patients who have central nervous system problems, such as movement and balance, coordination and feeling problems because those problems may be similar to chemotherapy induce peripheral neuropathy (CIPNs), which may effect on the result of the study.
- Patients who have skin infection, scar tissue, inflammation, and incision in the hand and ankle because all of them may effect on the patient ability to tolerate the cold therapy.
- Patients who have chronic disease as diabetes mellitus, hypertension, because those diseases may induce symptoms like CIPNs, and this may effect on the result of the study.
- Patients who have intolerance too cold as this condition may influence on the patient ability to apply cold therapy.

Sampling technique:

Based on the previous studies that examined the effect of cold therapy and exercise on chemotherapy induce peripheral neuropathy, the average sample size will be 100 to achieve 90% power to detect this difference with confidence level 95% based on this formula

Instruments of data collection:

Based on the review of relevant literature three instruments were used by the researcher for data collection, these instruments were:

- Instrument 1: Structured interview questionnaire.
- Instrument 2: Total neuropathy score (TNS).
- Instrument 3: Observational checklist.

Instrument I: Structured interview questionnaire:

This instrument was developed by the researcher to assess sociodemographic and medical data that include two parts:

- **Part one**: **Sociodemographic data**: It composed of patient's age, sex, occupation, marital status, occupation and educational level.
- **Part two**: **Medical data**: It composed of patient's past and present medical data such as presence of chronic disease, previous surgery, previous chemotherapy administration, primary diagnosis, duration of disease, disease stage, and current treatment (chemotherapy drug name, cycles of treatment, dose received and total number of doses).

Instrument II: Total Neuropathy Score (TNS):

It was developed by (Cornblath et al., 1999) to assess chemotherapy induced peripheral neuropathy. This instrument consists of 7 items (sensory symptoms, motor symptoms, autonomic symptoms, pin sensation, Vibration sensibility, Strength, deep tendon reflex) that assessed in a Likert type scale. Each item take a degree from 0-4. The total score of the scale range from 0- 28 and graded to four grade as in the following table.

Interpretation of total scoring system:

Grade of peripheral neuropathy	Score
Grade 1	1–7
Grade 2	8– 14
Grade 3	15–21
Grade 4	>21

Inter and intra rater reliability of the TNS was excellent (0.966 and 0.986 respectively). The cross-sectional validation study showed excellent correlations among all measures of neuropathy (Smith et al., 2010).

Instrument III: Observational Checklist.

It was developed by the researcher to evaluate patients' performance to the exercise program which include stretching and strenghthing exercise to feet,hand and arms (foot dorsiflexion, foot plantar flexion, gastrocnemius stretching, hamstring stretching, quadriceps exercises, biceps, and hand flexion-extension) followed by balance exercises to hip and knee (hip flexion,

hip extension, hip abduction, and knee flexion). The researcher checked if it practiced effectively or not by the patients. Each step of the exercise had three alternative responses as follow, two marks were given for performing each step in the exercise correctly. One mark was given for performing each step in the exercise correctly but incomplete. Zero was given for not performing the step in the exercise. All marks were summed and had score from 0 to 60, and converted into percentage. This score was categorized by the researcher as following 80% or more (48-60) indicate good performance, score between 50 % and less than 80% (30-47) indicate acceptable performance, score less than 50% (0-29) indicate bad performance.

Validity:

All instruments were tested for its content validity by jury of 5 experts in the field of Medical Surgical Nursing and Oncology Medicine and modification was done to ascertain relevance and completeness.

Reliability:

The first instruments were tested for reliability using a test retest method and a person correlation coefficient formula was used. The period between both tests was two weeks and the results were 0.97 for the first instrument and 0.91 for the fourth one. While second instruments were proved to be valid and reliable (Smith et al., 2010)

Pilot study:

A pilot study was conducted prior to data collection on 10% of the study sample (10 patients) to test the feasibility, clarity and applicability of the instruments then necessary modifications were done so these patients were excluded from the study sample.

Ethical Considerations:

- An approval from Ethical and research committee of the Faculty of Nursing, Menoufia University was obtained. Permission to carry out the study from responsible authorities after explanation of the purpose of the study was obtained.
- A written and oral consent was obtained from all subjects who met the inclusion criteria and agreed to participate in the study after explanation the purpose of study. Each subject was reassured that any obtained information would be confidential and would only be used for the study purpose. The researcher emphasized that participation in the study was entirely voluntary and anonymity of the subjects were assured through coding data. Subjects were also informed that they can withdraw from the study at any time without penalty and refusal to participate wouldn't affect their care. Moreover they were assured that the nature of the questionnaire didn’t cause any physical or emotional harm to them.

Data collection:

- Data collection was extended over a period of 8 months from the first of September 2023 to end of May 2024.
- Subjects who agreed to participate in the study and fulfilled the inclusion criteria were interviewed individually by the researcher at the

oncology department at Menoufia University Hospital, in chemotherapy administration room.

- The purpose of the study was explained to each study and control group.
- The study was conducted on four phases as follow: assessment, planning, implementation, and evaluation phases.

Assessment phase

- During this phase the researcher interviewed each subject of both groups to collect base line data by using the first three instruments (first, second instrument) and took about 30-45 minutes as follow:
- All subjects of both groups were assessed for sociodemographic data, medical data using instrument I (structured interview questionnaire) and assessed for sign and symptoms of peripheral neuropathy induced by chemotherapy using instrument II.

Planning phase

- Based on the baseline data that gathered from all patients and the review of related literature a coloured instructional booklet with illustrative pictures was prepared to be given to patients in the study group which include information about (Definition of chemotherapy, indications, methods of application, side effects, introduction of nervous system, component, effect of chemotherapy on nervous system, peripheral neuropathy definition, causes, signs& symptoms, complications, how to protect from it, and management which include pharmacological, surgical and non-pharmacological treatment) related to managing chemotherapy induced peripheral neuropathy.

Implementation phase

- During this phase, the researcher was conduct two session for the study group to apply the cold therapy and teach them how to do the exercise, each session took about 45-60 minutes.

❖ **During the first session**

- the researcher was explained to the patient the theoretical parts in the booklet and teach them how to apply the cold therapy and perform the exercise.
- At the end of the session, the researcher made conclusion and took feedback from each patient and the educational booklet given to the study group only.
- Cold application was applied by the researcher when the patients come to the hospital before the administration of chemotherapy drug by 30 minutes.
- The researcher was applied the cold gel pack to the patient for 30 minutes before the administration of chemotherapy drug and the patient or his relative was applied it for 60 minutes after chemotherapy administration.
- The cold gel was kept in the oncology department refrigerator to keep it cold to be administered after the session of chemotherapy.
- The researcher was assessed the area to be treated for infection, scar tissue, inflammation, and incision.
- Application area was exposed, and the patient assume the proper

position and the patient's privacy was maintained.

- Cold gel packs was used in the sizes of 30 cm × 20 cm for ankles and 20 cm × 10 cm for wrists.
- The cold gel pack was kept in (−20°C/−30°C) before using and the temperature was assessed by the thermometer.
- The application areas was wrapped with non-sterile gauze compress (10 cm × 10 cm) to prevent direct contact with cold.
- The cold pack was changed if the temperature increased to maintain optimal vasoconstrictive hypothermic conditions.
- During cold therapy application a period of temporary interruption was allowed for the patient according to their tolerance.
- Cold application was continued for 12 weeks.
- In addition to cold application the researcher demonstrated the exercise program to the patients for application at home.
- The exercise program was first started in the form of strengthening and stretching exercises (foot dorsiflexion, foot plantar flexion, gastrocnemius stretching, hamstring stretching, quadriceps exercises, biceps, and hand flexion-extension) followed by balance exercises (hip flexion, hip extension, hip abduction, and knee flexion).
- Exercise programme was practiced for 15-30 minutes as 5 times per week and continued for 12 weeks.
- The program was started by 10 repetitions for the first 3 weeks, the repetitions increased to 20 for (4, 5, and 6) weeks, and to 30 repetitions from the 7 to the end of twelve weeks to the strengthing and balancing exercise.

❖ **During the second session:**

- The participant in the study group (II) redemonstrated the exercise and the researcher evaluated their performance using instrument IV and response to any questions from the patients. It took about 30-45minutes.
- During follow up which continue for 12 weeks period the researcher was interviewed with the patients during chemotherapy session and ensure that they perform exercise and apply the cold therapy efficiently. It took about 30-45minutes.

Evaluation Phase

- Each subject in the study and the control group was assessed and evaluated three times; the first time in the assessment phase (pre intervention) at the first interview with the subjects using instrument I and II. The second time after 6 weeks from the first interview using instrument II, the third time after 12 weeks from the first interview using instrument II. The researcher was evaluated the performance of the study group to the exercise using instrument IV at the second session then at the 6 weeks and finally at 12 weeks.
- The comparison was done between the study group (I) and control group (II) to determine the effect of evidence-based practice on chemotherapy induced peripheral neuropathy.

Statistical analysis

Data was entered to the computer and analyzed using IBM SPSS software package version 21. Qualitative data was described using numbers and percentage. Quantitative data was described using range (minimum and maximum), mean and standard deviation. Significance of the obtained results was judged at the 5% level.

Two types of statistics were done:

i. Descriptive statistics:

They were expressed as mean and standard deviation (X+SD) for quantitative data or number and percentage (No & %) for qualitative data.

ii. Analytic statistics:

1) **Chi-square test**: For categorical variables, to compare between different groups.
2) **Fisher's Exact or Monte Carlo correction:** Correction for chi-square when more than 20% of the cells have expected count less than 5
3) **Marginal Homogeneity Test**: Used to analyze the significance between the different stages
4) **Student t-test**: For normally distributed quantitative variables, to compare between two studied groups
5) **Paired t-test**: For normally distributed quantitative variables, to compare between two periods
6) **Correlation coefficient (r)**: For normally distributed quantitative variables to compare between variables

P-value at 0.05 was used to determine significance regarding:

- P-value > 0.05 to be statistically insignificant.
- P-value ≤ 0.05 to be statistically significant.
- P-value ≤ 0.001 to be highly statistically significant.

Results

Table (1) reveal distribution of study and control group regarding their past medical history. This table illustrates that a history of chronic diseases was present in 12% of the study group and 26% of the control group. Chest allergy representing 50% and 53% of the study and control group respectively. As regard to previous surgery, 22% of the study and 28% of the control group had previous surgery, 63.6% of the study and 42.9% of the control had appendectomy. All of the study and the control group didn't had chemotherapy before (100% and 100% respectively). There were no statistically significant differences between the study and control groups regarding previous medical history.

Table (2) reveals distribution of study and control group regarding their present medical history. This table illustrate that the mean and stander deviation of the onset of the disease were 5.48 ±2.77 for the study and 6.04±2.24 for the control group. About half 52% of the study group and about three quarter of control group (76%) had cancer stage II. Regarding to type of chemotherapy nearly half 42% of the study and 48% of the control group were receive taxol. More than three quarter(80%) of both studied group had onset of the disease from month to less than 6 months. Concerning time

between cycle of chemotherapy treatment, more than three quarter 78% of the study and more than two third 70% of control group were received chemotherapy treatment every 21 day. The mean and stander deviation of the number of chemotherapy doses for both study and control group were 8.08 ±3.06 and 9.20 ±2.39 respectively.

Table (3) This table shows that, the patients in the study group had highly statistical significant difference regarding to their total neuropathy level between pre and after 6 weeks of intervention, between after 6 weeks and after 12 weeks of intervention and between pre and after 12 weeks of intervention with P value(0.000**, 0.016* and .000** respectively).

Table (4) This table shows that there was highly statistical significant negative correlation between total performance of the exercise and total neuropathy post intervention (after 6 weeks) with p value 0.000** and significant negative correlation at follow up after (12 weeks) with p value 0.006*.

Figure (1) this figure revealed that 64% of the study group had grade 2 of neuropathy at pre intervention compared with 68% and 88% had grad 1 of neuropathy post intervention and at follow up respectively. On the other hand, 68% of the control group had grade 2 of neuropathy at pre intervention compared with 32% and 36% had grad 1 of neuropathy post intervention and at follow up respectively. There were highly statistically significant difference between the study and the control group in regard to the total neuropathy score after six and 12weeks of the intervention with p value 0.001**& 0.000** respectively.

Table (1): Distribution of study and control group regarding their past medical history (n=100).

Past medical History	Study (n=50)		Control (n=50)		X^2	p-value
	No	%	No	%		
Presence of chronic disease						
▪ Yes	6	12.0	13	26.0	3.18	0.074
▪ No	44	88.0	37	74.0		
Types of chronic disease						
▪ Renal disease	2	33.3	2	15.4	1.18	0.757
▪ Cardiac disease	1	16.7	3	23.1		
▪ Chest allergy	3	50.0	7	53.8		
▪ Liver disease	0	0.0	1	7.7		
Previous surgery						
▪ Yes	11	22.0	14	28.0	0.48	0.488
▪ No	39	78.0	36	72.0		
Types of surgery performed						
▪ Cholecystitis	3	27.3	7	50.0	1.34	0.513
▪ Appendectomy	7	63.6	6	42.9		
▪ Cardiac splent	1	9.1	1	7.1		
Previous chemotherapy treatment						
▪ Yes	0	0.0	0	0.0	.000	1.000
▪ No	50	100.0	50	100.0		

Table (2): Distribution of study and control group regarding their present medical history (n=100).

Present medical history	Study (n=50)		Control (n=50)		Test of significant	
	No	%	No	%	X^2	p-value
Duration of disease						
▪ <5	17	34.0	10	20.0		
▪ 5-<10	30	60.0	36	72.0	2.50	0.286
▪ 10 and more	3	6.0	4	8.0		
Mean ±SD	5.48±2.77		6.04±2.24		t-test =1.46	0.147
Tumor stage						
▪ First	11	22.0	6	12.0		
▪ Second	26	52.0	38	76.0	7.19	0.066
▪ Third	11	22.0	6	12.0		
▪ Fourth	2	4.0				
Type of chemotherapy						
▪ Taxol	21	42.0	24	48.0		
▪ Fluracil	4	8.0	7	14.0		
▪ Gemizar	4	8.0	8	16.0		
▪ Vincristine	4	8.0	5	10.0	8.95	0.256
▪ Oxiplatine	3	6.0	2	4.0		
▪ Haloxan	5	10.0	2	4.0		
▪ Carpoplatin	6	12.0	2	4.0		
▪ Adryamicin	3	6.0	0	0.0		
Duration of taking chemotherapy treatment						
▪ Less than 1 month	5	10.0	3	6.0	2.32	0.509
▪ 1 month to less than 6 months	40	80.0	40	80.0		
▪ 6 months to less than year	4	8.0	0	0.0		
▪ More than year	1	2.0	7	14.0		
Time between cycles of chemotherapy treatment						
▪ Every15 day	9	18.0	13	26.0	0.94	0.624
▪ Every 21 day	39	78.0	35	70.0		
▪ Every month	2	4.0	2	4.0		
Number of chemotherapy doses that taken						
▪ <5	4	8.0	1	2.0		
▪ 5-<10	35	70.0	29	58.0	4.98	0.083
▪ 10 and more	11	22.0	20	40.0		
Mean ±SD	8.08±3.06		9.20±2.39		t-test 1.507	0.147

Figure (1): Percentage distribution of study and control group regarding their total neuropathy level through the study period.

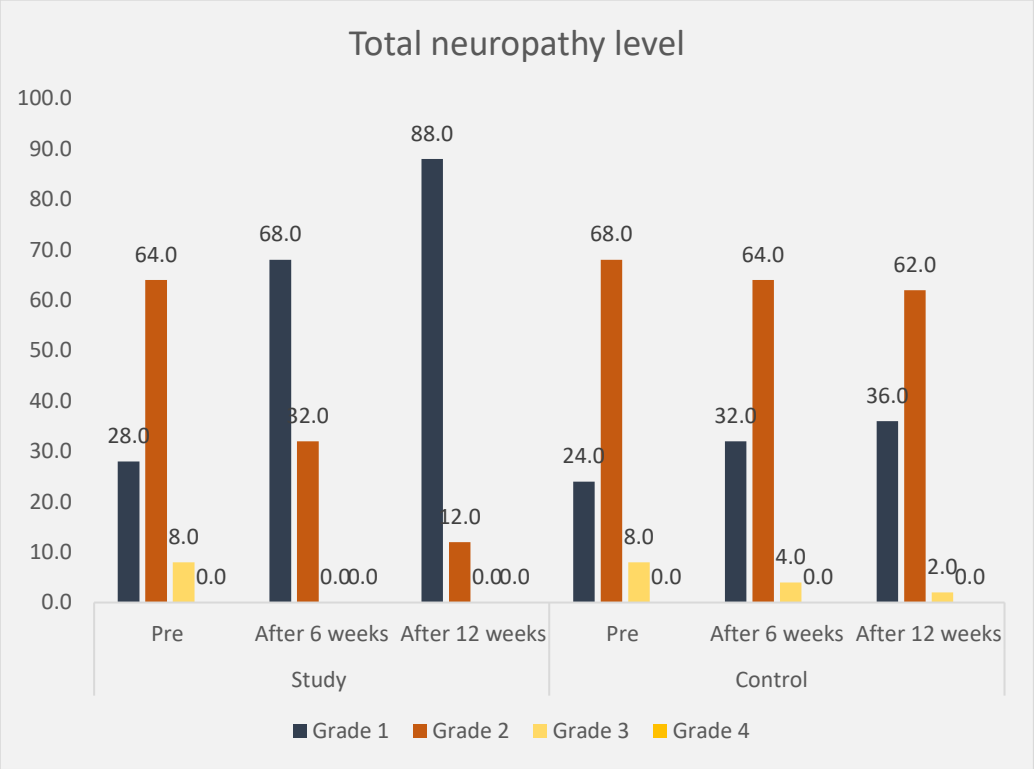

Table (3): Distribution of study group regarding their total neuropathy level through the study period.

Total neuropathy level	Study group						X^2	p-value
	Pre intervention		Post intervention after 6 weeks		Follow up after 12 weeks			
	No	%	No	%	No	%		
▪ Grade 1	14	28.0	34	68.0	44	88.0	17.66	P1:0.000**
▪ Grade 2	32	64.0	16	32.0	6	12.0	5.82	P2:0.016*
▪ Grade 3	4	8.0	0	0.00	0	0.00	37.30	P3:0.000**
▪ Grade 4	0	0.0	0	0.00	0	0.00		

P1: between pre and after 6 weeks of intervention

P2: between after 6 weeks and after 12 weeks of intervention

P3: between pre and after 12 weeks of intervention

* statistically significance p<.05 **Highly statistically significance p<.001

Table (4): Correlation between total exercise performance and total neuropathy through the study period

Total neuropathy score	Total exercise performance	
	r	p-value
▪ Pre intervention	-0.138	.340
▪ Post intervention after 6 weeks	-0.477	.000**
▪ Follow up after 12 weeks	-0.386	.006*

Discussion

CIPN is among the most prevalent and debilitating adverse effects of cancer treatment. Approximately 60% of cancer survivors develop CIPN from neurotoxic chemotherapies, such as taxanes (paclitaxel, docetaxel), platinums (oxaliplatin, cisplatin, carboplatin), vinca alkaloids (vincristine, vinblastine, vinorelbine), bortezomib, and antiangiogenesis agents (thalidomide, lenalidomide). These chemotherapies can damage the peripheral sensory, motor, and autonomic nerves and lead to CIPN manifestations, most commonly numbness, tingling, burning or shooting pain, extremity weakness, and loss of proprioception and deep tendon reflexes. Long-term pain and sensorimotor deficits associated with CIPN increase risk of falls and impair physical function and quality of life (QOL). Thus, CIPN is a primary dose-limiting factor for patients who are receiving neurotoxic chemotherapy for the treatment of their cancer (Souza et al 2023).

In relation to presence of chronic disease, the current study shows that the majority of the studied group hadn't chronic disease. This finding is supported by Chaywiriyangkool et al., (2022) who studied "Cryotherapy for Preventing Chemotherapy Induced Peripheral Neuropathy in Patients with Gynecologic Cancer in Thammasat University Hospital" at Thailand and reported that about two third of the studied group had chronic disease and about half of them had hypertention. On the other hand, this finding contradicated with Beijers et al., (2020) who studied the "Multicenter randomized controlled trial to evaluate the efficacy and tolerability of frozen gloves for the prevention of chemotherapy-induced peripheral neuropathy" demonstrated that the majority of the studied groups have chronic disease and most of them had hypertension. From the researcher point of view, the difference in the result of the study related to the inclusion and exclusion criteria of the study as we exclude any chronic disease which may effect on the result of the study.

Concerning to the previous surgery, the result of the present study found that less than one third of the studied groups have not previous surgery. This was in consistent with Gui et al., (2021) who study "Efficacy of Exercise Rehabilitation Program in Relieving Oxaliplatin Induced Peripheral Neurotoxicity" found that about two third of the studied group had previous surgery.

In concerning to previous receiving of chemotherapy, the result of the current study showed that both studied groups hadn't received chemotherapy before. This result is contradicted by with shaheen et al., (2020) who study "Chemotherapy-Induced Peripheral Neuropathy and its Impact on Health-Related Quality of Life among **Multiple Myeloma Patients**: A Single-Center Experience" in Kingdom of Saudi Arabia and reported that about one third of the studied groups receive chemotherapy before. From the researcher point of view, the difference is related to all the studied group had

the disease for the first time and also receives chemotherapy for the first time.

In relation to diagnosis, the results of the current study mentioned that about half of the study group has breast cancer. This result is consistent with Ting bao et al., (2021) who conduct a study entiteled "Health-Related Quality of Life in Cancer Survivors with Chemotherapy-Induced Peripheral Neuropathy: A Randomized Clinical Trial" in New york, and reported that about half of the study group has breast cancer. Additionally, Beijers et al., (2020) who found that more than half of the study group have colorectal cancer. Also, Gui et al., (2021) who stated that more than half of the study group have colorectal cancer. From the researcher point of view, the result of the study is related to about two third of the studied groups were female and breast cancer is more common among female than male.

As regarding to tumor stage, the result of the study reveal that about half of the study group were at the second stage of the disease. This finding is similar to study conducted in USA by Kleckner et al., (2021) entitled "Longitudinal study of inflammatory, behavioral, clinical, and psychosocial risk factors for chemotherapy-induced peripheral neuropathy" and mentioned that about half of the study group were at the second stage of the disease. In addition, a study that was done by Ting bao et al., (2021) who reported also that about half of the study group were at the second stage of the disease. This was inconsistent with Xu et al., (2023) who carried a study in china study the "Efficacy of cryotherapy on chemotherapy-induced peripheral neuropathy in patients with breast cancer" and found that about one third of the study group was at the second stage of the disease. Also, these finding are similar to study conducted in canada by Kirkham et al., (2020) entiteled "Chemotherapy-periodized" Exercise to Accommodate for Cyclical Variation in Fatigue" and showed that about half of the study group were at the second stage of the disease.

In relation to type of chemotherapy, the result of the current study reveals that about half of the study group receive taxol as chemotherapy medication. These results agree with Kleckner et al., (2021), who showed that about two third of the studied group receive taxan. Also, these findings were in the same line with Sturgeon et al., (2022) who conducted a study in USA about "Feasibility of a tailored home-based exercise intervention during neoadjuvant chemotherapy in breast cancer patients: clarfied that most of the studied groups receive taxol. While these finding are contradicated by Beijers et al., (2020) who reported that about two third of the studied groups receive oxiplatine. Additionally, Shaheen et al., (2020) who found that about two third of the studied group received Bortezomib-cyclophosphamide. From the researcher point of view, this is related to the neuropathy is more common among patient receive taxole as it is the most medication cause neuropathy.

In relation to number of cycle received, the result of this study revealed that the mean and standard

deviation is (8.08± 3.06) for the study group. This is consistent with Saykal et al., (2024) who conducted a study in turkey about "The Effect of Peripheral Neuropathy on Disability and Anxiety" and showed that the mean and standard deviation is (10.50 ±6.00) for the study group. Also, these findings are supported by Visovsky et al., (2024) whose study about "Fall Risk Associated with Taxanes: Focus on Chemotherapy-Induced Peripheral Neuropathy" at University of South Florida and reported that the mean and standard deviation is (7.193±.77). In addition to, a study done by Mallik, et al., (2024) about "Incidence, Severity, and Clinical Correlations of Oxaliplatin-Induced Neuropathy in Patients with Colorectal Cancer: A Single-Institution Experience from Northeast India" at India and revealed that the mean and standard deviation is (8.91 ± 2, 6). On the other hand this finding is inconsistent with Xu et al., (2023) who demonstrated that the mean and standard deviation was (3.97±2.35). Additionally, Beijers et al., (2021) clarified that the mean and standard deviation was (5.7± 2.1). From the researcher point of view, the number of chemotherapy cycle depends on the stage and severity of the disease.

Regarding to level of chemotherapy induced peripheral neuropathy for both study and control groups throughout study periods, the result of the current study presented that there were highly statistically significant difference between studied groups in regard to the total neuropathy score after six and 12weeks of the intervention with p value .001**& .000** respectively. This finding are similer to the study conducted in Newcastle University Centre for Cancer, Newcastle University, Newcastle-Upon-Tyne, UK by Brownson et al., (2023) who studied "Effect of exercise before and/or during taxane containing chemotherapy treatment on chemotherapy-induced peripheral neuropathy symptoms in women with breast cancer: systematic review and meta-analysis". Who reported that the total neuropathy level had decreased in the study group who exercised before and/or during taxane-based chemotherapy versus the control group. Also, the study conducted by Saint et al., (2024) entiteled "Impact of exercise on chemotherapy-induced peripheral neuropathy in survivors with post-treatment primary breast cancer" at University of Michigan Medical School, USA reported that exercise was associated with reduced prevalence of all CIPN symptoms regardless of chemotherapy type with $p < 0.001$.

Additionally, these result come in accordance with a study conducted by Crichton, et al., (2022) at Australia who studied" Non-Pharmacological Self-Management Strategies for Chemotherapy-Induced Peripheral Neuropathy in People with Advanced Cancer: A Systematic Review and Meta-Analysis" and reported that the strongest evidence with the most certainty was found for physical exercise as a safe and viable adjuvant to chemotherapy treatment for the prevention and management of CIPN and related physical function in people with advanced cancer. Also, these

findings agree with Vigano et al., (2024) who conducted a study in Canada about "Impact of Cannabidiol and Exercise on Clinical Outcomes and Gut Microbiota for Chemotherapy-Induced Peripheral Neuropathy in Cancer Survivors: A Case Report" and showed that the combined CBD and multi-modal exercise (MME) intervention was most beneficial and well tolerated and not only improveme all functional measures and the largest reduction in pain score but also showed clinically meaningful improvements in CIPN symptoms.

Moreover, Tai et al., (2024) mentioned in their study about" Efficacy of cryotherapy in the prevention of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis" at College of Medicine, Taipei Medical University, Taipei, Taiwan that Cryotherapy demonstrates a pronounced preventive effect against the development of CIPN, providing substantial symptomatic relief and quality of life improvements for patients undergoing chemotherapy. Also, this finding coincides with Chaywiriyangkool et al., (2022) who studied "Cyotherapy for preventing chemotherapyInduced peripheral neuropathy in patients with gynecologic cancer in Thammasat University Hospital", in Thammasat University, Pathum Thani, Thailand and reported that cryotherapy was effective in management of CIPN and prevented loss of tactile sensation, temperature sensation and vibration perception. Also, a study done by Şimşek and Demir, (2021) entiteled "Cold Application and Exercise on Development of Peripheral Neuropathy during Taxane Chemotherapy in Breast Cancer Patients: A Randomized Controlled Trial" conducted with at Department of Nursing, Faculty of Health Sciences, Ankara University, Ankara, Turkey, and indicated that exercise and cold application were effective in the management of CIPN.

While, these finding are contradicated by Accordino et al., (2024) who study "Randomized adaptive selection trial of cryotherapy, compression therapy, and placebo to prevent taxane-induced peripheral neuropathy in patients with breast cancer" at Columbia University Medical Center, New York, USA and reported that Compression therapy was the most effective intervention in the management and prevention of chemotherapy induced peripheral neuropathy than cold therapy. Also, a study done by Ng et al., (2020) who study "Impact of Cryotherapy on Sensory, Motor, and Autonomic Neuropathy in Breast Cancer Patients Receiving Paclitaxel: A Randomized, Controlled Trial" conducted at National Cancer Centre Singapore, and mentioned that there was insufficient evidence that cryotherapy prevents sensory neuropathy which may be due to the high rates of cryotherapy interruption in this study. From the researcher point of view, cold therapy and exercise was effective in improving chemotherapy induced peripheral neuropathy as the exercise strength the muscle and improve physical function for the patients and application cold therapy lead to vasoconstriction of blood vessels and prevent the effect of

chemotherapeutic drugs on the extremities.

The present study shows that there was highly statistical significant negative correlation between total exercise performance and total neuropathy post intervention after 6 weeks and significant negative correlation at follow up after 12 weeks. These findings are in line with Nakagawa et al.,(2024) who study "Exercise intervention for the management of chemotherapy-induced peripheral neuropathy: a systematic review and network meta-analysis" in Japan and reported that, the exercise intervention have beneficial effect on managing the chemotherapy induced peripheral neuropathy symptoms and was recently highlighted by asystematic review. From the researcher point of view, good performance to the exercise program lead greater effect of the exercise on the muscle, strengthen the extremities, increasing the supply of blood, glucose, and oxygen to mitochondria and as a result reducing neuropathic symptoms and by the way reduce the total neuropathy score.

Conclusion

Chemotherapy induced peripheral neuropathy is an important problem for cancer patients and survivors due to its high prevalence among cancer patients. Evaluation of peripheral neuropathy, which has a negative effect on the cancer treatment process, and its early diagnosis and enhancement of patients' quality of life are important for assuring the sustainability of the treatment

Furthermore, the results highlight the effectiveness of exercise and cold therapy in improving the neuropathy symptoms and activity of daily living among patients receiving chemotherapy

Recommendations

Based on the findings of the current study, the following recommendations are derived and suggested:

A. Recommendation for patients:

- Supervised health teaching program should be carried out for all cancer patients from the beginning of the chemotherapy medication about the importance of exercise and cold therapy to reduce CIPN and improve their activities of daily living and a colored booklet should be available and distributed about disease.

B. Recommendation for research:

- Replication of the study with three groups (first group implement exercise therapy, the second group applying cold therapy and the control group) to assess the effectiveness of each intervention alone.

Reference

Kunutsor, S. K., Lehoczki, A., & Laukkanen, J. A. (2024). The untapped potential of cold water therapy as part of a lifestyle intervention for promoting healthy aging. GeroScience, 1-21.

Lin, W. L., Wang, R. H., Chou, F. H., Feng, I. J., Fang, C. J., & Wang, H. H. (2021). The effects of exercise on chemotherapy-induced peripheral neuropathy symptoms in cancer patients: a systematic review and meta-

analysis. Supportive Care in Cancer, 29, 5303-5311.

Liampas, A., Rekatsina, M., Vadalouca, A., Paladini, A., Varrassi, G., & Zis, P. (2021). Pharmacological management of painful peripheral neuropathies: a systematic review. Pain and Therapy, 10, 55-68.

Kunutsor, S. K., Lehoczki, A., & Laukkanen, J. A. (2024). The untapped potential of cold water therapy as part of a lifestyle intervention for promoting healthy aging. GeroScience, 1-21.

Mattar, M., Umutoni, F., Hassan, M. A., Wamburu, M. W., Turner, R., Patton, J. S., ... & Lei, W. (2024). Chemotherapy-induced peripheral neuropathy: a recent update on pathophysiology and treatment. Life, 14(8), 991.

Gewandter, J. S., Kleckner, A. S., Marshall, J. H., Brown, J. S., Curtis, L. H., Bautista, J., ... & Mustian, K. M. (2020). Chemotherapy-induced peripheral neuropathy (CIPN) and its treatment: an NIH Collaboratory study of claims data. Supportive Care in Cancer, 28, 2553-2562.

Dhawan, S., Andrews, R., Kumar, L., Wadhwa, S., & Shukla, G. (2020). A randomized controlled trial to assess the effectiveness of muscle strengthening and balancing exercises on chemotherapy-induced peripheral neuropathic pain and quality of life among cancer patients. Cancer Nurs.;43(5):269–80.

John, L., Dobson, L., Jim, M., & Li, L. (2018). Benefits of exercise intervention in reducing neuropathic pain. Neurosci; 8(2):102.

Cornblath, D., Chaudhry, V., Carter, K. (1999). Total neuropathy score: validation and reliability study. Neurology;53(8):1660-64.

Mahoney, F& Barthel, D. (1965). Functional evaluation: the Barthel Index. MD State Med J;14(4):61–5.

Ferfeli, S., Galanos, A., Dontas, I. A., Triantafyllou, A., Triantafyllopoulos, I. K., & Chronopoulos, E. (2023). Reliability and validity of the Greek adaptation of the modified Barthel Index in neurorehabilitation patients. European Journal of Physical and Rehabilitation Medicine, 60(1), 44.

Smith, E. M. L., Cohen, J. A., Pett, M. A., & Beck, S. L. (2010). The reliability and validity of a modified total neuropathy score-reduced and neuropathic pain severity items when used to measure chemotherapy-induced peripheral neuropathy in patients receiving taxanes and platinums. Cancer nursing, 33(3), 173-183.

Souza, R. S., Alvarez, G. A. M., Dombovy-Johnson, M., Eller, J., & Abd-Elsayed, A. (2023). Evidence-based treatment of pain in chemotherapy-induced peripheral neuropathy. Current

Pain and Headache Reports, 27(5), 99-116.

Brownson-Smith, R., Orange, S. T., Cresti, N., Hunt, K., Saxton, J., & Temesi, J. (2023). Effect of exercise before and/or during taxane-containing chemotherapy treatment on chemotherapy-induced peripheral neuropathy symptoms in women with breast cancer: systematic review and meta-analysis. Journal of Cancer Survivorship, 1-19.

Saint, K., Nemirovsky, D., Lessing, A., Chen, Y., Yang, M., Underwood, W. P., ... & Bao, T. (2024). Impact of exercise on chemotherapy-induced peripheral neuropathy in survivors with post-treatment primary breast cancer. Breast Cancer Research and Treatment, 1-9.

Crichton, M., Yates, P. M., Agbejule, O. A., Spooner, A., Chan, R. J., & Hart, N. H. (2022). Non-pharmacological self-management strategies for chemotherapy-induced peripheral neuropathy in people with advanced cancer: a systematic review and meta-analysis. Nutrients, 14(12), 2403.

Vigano, M., Kubal, S., Lu, Y., Habib, S., Samarani, S., Cama, G., ... & Costiniuk, C. T. (2024). Impact of Cannabidiol and Exercise on Clinical Outcomes and Gut Microbiota for Chemotherapy-Induced Peripheral Neuropathy in Cancer Survivors: A Case Report. Pharmaceuticals, 17(7), 834.

Accordino, M. K., Lee, S., Leu, C. S., Levin, B., Trivedi, M. S., Crew, K. D., ... & Hershman, D. L. (2024). Randomized adaptive selection trial of cryotherapy, compression therapy, and placebo to prevent taxane-induced peripheral neuropathy in patients with breast cancer. Breast Cancer Research and Treatment, 204(1), 49-59.

Tai, H. Y., Lin, L. Y., Huang, T. W., & Gautama, M. S. N. (2024). Efficacy of cryotherapy in the prevention of chemotherapy-induced peripheral neuropathy: A systematic review and meta-analysis. Supportive Care in Cancer, 32(7), 482.

Chaywiriyangkool, C., Thaweekul, Y., Poomtavorn, Y., Mairaing, K., Punyashthira, A., Wisarnsirirak, P., ... & Suwannarurk, K. (2022). Cryotherapy for Preventing Chemotherapy-Induced Peripheral Neuropathy in Patients with Gynecologic Cancer in Thammasat University Hospital. Science & Technology Asia, 144-151.

Ng, D. Q., Tan, C. J., Soh, B. C., Tan, M. M. L., Loh, S. Y., Tan, Y. E., ... & Loh, K. W. J. (2020). Impact of cryotherapy on sensory, motor, and autonomic neuropathy in breast cancer patients receiving paclitaxel: a randomized, controlled trial. Frontiers in neurology, 11, 604688.

Dhawan, S., Andrews, R., Kumar, L., Wadhwa, S., & Shukla, G. (2020). A randomized controlled trial to assess the effectiveness of

muscle strengthening and balancing exercises on chemotherapy-induced peripheral neuropathic pain and quality of life among cancer patients. Cancer nursing, 43(4), 269-280.

Ragab, I. I., Wahman, M. M., Bu Aqoulah, E. A., Alhalabi, M. N., Jabir, M. A., & Atef, A. M. (2024). Effect of Implementing Bundle of Care on Breast Cancer Patients Paclitaxel Induced Peripheral Neuropathy and Quality of Life. Tanta Scientific Nursing Journal, 33(2), 287-309.

Shaheen, N. A., Alqahtani, M., Alawbthani, N. S., Thomas, A., & Alaskar, A. (2020). Chemotherapy-induced peripheral neuropathy and its impact on health-related quality of life among multiple myeloma patients: a single-center experience. Indian Journal of Palliative Care, 26(4), 506.

Gui, Q., Li, D., Zhuge, Y., & Xu, C. (2021). Efficacy of exercise rehabilitation program in relieving oxaliplatin induced peripheral neurotoxicity. Asian Pacific Journal of Cancer Prevention: APJCP, 22(3), 705.

Cao, A., Cartmel, B., Li, F. Y., Gottlieb, L. T., Harrigan, M., Ligibel, J. A., ... & Ferrucci, L. M. (2023). Effect of Exercise on Chemotherapy-Induced Peripheral Neuropathy among patients treated for Ovarian Cancer: a secondary analysis of a Randomized Clinical Trial. JAMA network open, 6(8), e2326463-e2326463.

TingBao, T., Baser, R., Chen, C., Weitzman, M., Zhang, Y. L., Seluzicki, C., ... & Zhi, W. I. (2021). Health-related quality of life in cancer survivors with chemotherapy-induced peripheral neuropathy: a randomized clinical trial. The Oncologist, 26(11), e2070-e2078.

Nakagawa, N., Yamamoto, S., Hanai, A., Oiwa, A., & Arao, H. (2024). Exercise intervention for the management of chemotherapy-induced peripheral neuropathy: a systematic review and network meta-analysis. Frontiers in Neurology, 15, 1346099

Xu, M., Wang, F., Zhu, X., & Hao, Z. (2023). Efficacy of cryotherapy on chemotherapy-induced peripheral neuropathy in patients with breast cancer: a propensity score-matched study. Annals of Medicine and Surgery, 85(6), 2695-2703.

Gewandter, J. S., Kleckner, A. S., Marshall, J. H., Brown, J. S., Curtis, L. H., Bautista, J., ... & Mustian, K. M. (2020). Chemotherapy-induced peripheral neuropathy (CIPN) and its treatment: an NIH Collaboratory study of claims data. Supportive Care in Cancer, 28, 2553-2562.

Barnes, S. (2024). A Multimodal Approach: Implementing OMM for Spinal Surgery Patients' Pain and Anxiety.

Maihöfner, C., Diel, I., Tesch, H., Quandel, T., & Baron, R. (2021).

Chemotherapy-induced peripheral neuropathy (CIPN): current therapies and topical treatment option with high-concentration capsaicin. Supportive Care in Cancer, 29, 4223-4238.

Sturgeon, K. M., Smith, A. M., Federici, E. H., Kodali, N., Kessler, R., Wyluda, E., ... & Schmitz, K. H. (2022). Feasibility of a tailored home-based exercise intervention during neoadjuvant chemotherapy in breast cancer patients. BMC Sports Science, Medicine and Rehabilitation, 14(1), 31.

Saykal, T. U., & Uysal, N. (2024). The Effect of Peripheral Neuropathy on Disability and Anxiety. Florence Nightingale Journal of Nursing, 32(1), 30.

Visovsky, C., Wodzinski, P. T., Haladay, D., Ji, M., & Coury, J. (2024, August). Fall risk associated with taxanes: focus on chemotherapy-induced peripheral neuropathy. In Seminars in oncology nursing (Vol. 40, No. 4, p. 151687). WB Saunders.

Mallik, S., Roy, P. S., Saikia, B. J., Hazarika, M., & Talukdar, A. (2024). Incidence, Severity and Clinical Correlation of Oxaliplatin Induced Neuropathy in Patients with Colorectal Cancer: A Single Institutional Experience. Asian Pacific Journal of Cancer Care, 9(1), 55-63.

Kirkham, A. A., Bland, K. A., Zucker, D. S., Bovard, J., Shenkier, T., McKenzie, D. C., ... & Campbell, K. L. (2020). " Chemotherapy-periodized" Exercise to Accommodate for Cyclical Variation in Fatigue. Medicine and science in sports and exercise, 52(2), 278-286.

Kleckner, I. R., Jusko, T. A., Culakova, E., Chung, K., Kleckner, A. S., Asare, M., ... & Mustian, K. M. (2021). Longitudinal study of inflammatory, behavioral, clinical, and psychosocial risk factors for chemotherapy-induced peripheral neuropathy. Breast cancer research and treatment, 189, 521-532.

Beijers, A. J. M., Bonhof, C. S., Mols, F., Ophorst, J., de Vos-Geelen, J., Jacobs, E. M. G., ... & Vreugdenhil, G. (2020). Multicenter randomized controlled trial to evaluate the efficacy and tolerability of frozen gloves for the prevention of chemotherapy-induced peripheral neuropathy. Annals of Oncology, 31(1), 131-136.

Abdollahi, A., Amirkhanloo, F., Karimi, G., Yousefi-Manesh, H., Roohbakhsh, A., & Dehpour, A. R. (2020). The protective effect of modafinil on vincristine-induced peripheral neuropathy in rats: a possible role for TRPA1 receptors. Basic & Clinical Pharmacology Toxicology, 127(5), & 405-418.