Original Article

Check for updates

pISSN 2383-6415 eISSN 2383-6423
www.bionursingjournal.or.kr
Journal of Korean Biological Nursing Science 2022;24(2):86-94
https://doi.org/10.7586/jkbns.2022.24.2.86

Factors that Affect Remission of Chemotherapy-Induced Peripheral Neuropathy Symptoms: Short-Term Prospective Study

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Purpose: Patients experiencing chemotherapy-induced peripheral neuropathy (CIPN) apply various palliative care as well as drugs in their daily life to alleviate symptoms. There is a need to identify the influence of these efforts and patients' psychosocial status on the relief of CIPN symptoms. This short-term prospective study investigated how prescription drugs, non-pharmacological behaviors (exercise, massage, and heat therapy), and psychological states (social support, depression, and anxiety) affected CIPN symptoms. **Methods:** Participants scheduled to receive postoperative platinum or taxane-based chemotherapy were enrolled consecutively. CIPN was measured with the Neurotoxicity-12 subscale of the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity-12 instrument. Data were collected three times during the 4 or 5 cycles of chemotherapy. **Results:** At the end of the 2nd chemotherapy cycle, 93.1% of participants reported CIPN symptoms. Multiple regression analyses showed that a heat therapy ($\beta = -.34$, $p < .001$), massage ($\beta = -.21$, $p = .012$), and walking 5 times or more per week ($\beta = -.26$, $p = .021$) provided relieve for CIPN symptoms. Depression ($\beta = .19$, $p = .027$) significantly exacerbated CIPN symptoms. **Conclusion:** These results suggested that a comprehensive management program that includes walking, heat therapy, massage, and mood therapy should be encouraged. Moreover, patients should be educated at chemotherapy initiation to understand appropriate interventions that can relieve CIPN symptoms.

Key Words: *Adjuvant chemotherapy; Peripheral nervous system diseases; Walking; Massage; Hot temperature*

INTRODUCTION

Due to early cancer detection and the development of new treatments, one in every 31 Koreans receives or survives cancer treatment. Although the cancer survival rate has increased, many survivors experience side effects from cancer treatment [1]. Neurotoxic anti-cancer drugs cause chemotherapy-induced peripheral neuropathy (CIPN), and progression of CIPN leads to impaired daily living activities and poor quality of life [2]. Therefore, health care professionals should play a critical role in assessing and managing CIPN [3].

The prevalence of CIPN symptoms is agent-dependent; the estimated prevalences were 70-100% for platinum-based drugs and 11-87% for taxanes [4]. In addition, CIPN can occur with either a high single dose or after cumulative exposure. CIPN symptoms typically occur and continue during chemotherapy, and they gradually improved after treatment ends. However, in some patients, the symptoms persist without improvement [5]. As a result, CIPN can negatively affect physical abilities, social functioning, and the emotional well-being of patients with cancer, during and after treatment [6,7].

Although the type and severity of CIPN symptoms depend on the

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*This manuscript is a condensed form of the first author's master's thesis.

Received: April 30, 2022 **Revised:** May 16, 2022 **Accepted:** May 27, 2022

type and cumulative dose of chemotherapeutic agents [8], CIPN symptoms can result in treatment delays, dose modifications, and in severe cases, treatment discontinuation [9]. Therefore, it is important to prevent or alleviate CIPN symptoms.

Many studies have examined the effects of pharmacologic and non-pharmacologic interventions. However, the evidence is insufficient on the effect of drugs (except duloxetine) on CIPN symptoms [10]. Moreover, studies on non-pharmacologic interventions, including exercise [11,12], acupuncture [13,14], massage [15], and footbaths [16] have provided insufficient evidence of their effects on alleviating CIPN symptoms [17]. In addition, studies showed that CIPN symptoms depended on the patient's psychosocial factors such as depression, anxiety, and perceived support [18,19].

Although no drug, except duloxetine, has been recommended for alleviating CIPN symptoms, various pain killers have been prescribed in the clinical field to alleviate the symptoms of peripheral neuropathy [10]. Moreover, in addition to prescription drugs, many patients have applied various non-pharmacological methods in lieu of medical advice [3]. Therefore, it is necessary to identify the comprehensive influence of pharmacological and non-pharmacological interventions, and psychosocial factors on CIPN symptom alleviation.

This study aimed to examine the comprehensive influence of prescription drugs, non-pharmacological interventions, and psychosocial factors on the alleviation of CIPN symptoms in everyday situations, rather than controlled experimental or hospital situations. We applied a short-term prospective design to clarify the temporal relationship between potential independent variables and CIPN symptoms. Our results could provide the basis for the development of comprehensive, effective nursing interventions for managing CIPN symptoms.

METHODS

1. Study design

This short-term, prospective descriptive study aimed to identify factors that affected the relief of CIPN symptoms in patients with cancer that received chemotherapy. Data were collected at three time points: the first was at the screening, and the other two time points were during chemotherapy cycles to assess the incidence and changes in CIPN symptoms.

2. Participants

The target population comprised patients with cancer that were scheduled to receive adjuvant chemotherapy after surgery. Study participants were selected from outpatients of a university hospital through consecutive sampling. Patient selection criteria were: 19 years of age or older; scheduled to receive platinum or taxane after surgery; able to communicate; and could understand the purpose of the study and agreed to participate in the study. In fact, participants of this study mainly received a combination chemotherapy. However, the degree of CIPN symptoms was not clinically different between patients treated with a single drug and those treated with a combination of drugs [20]. Therefore, we evaluated the effects of platinum and taxane in this study.

Patient exclusion criteria were: previously received chemotherapy or radiation therapy; a diagnosis of HIV, multiple sclerosis, spinal cord compression syndrome, spinal cord stenosis, diabetes, or pregnancy, to rule out other neuropathies; exposure to other neurotoxic substances; and a diagnosis of a mental, cognitive, or physical disorder.

We calculated the minimum number of samples required for a multiple regression analysis with the G*power 3.1 program. When we assumed 12 predictors, a significance level of .05, a power of .80, and a medium effect size of 0.15, a total of 127 participants were required. The final analysis included 130 samples.

3. Measurements

• *CIPN symptoms*: To assess CIPN symptoms, we implemented the Neurotoxicity-12 subscale (Ntx-12) of the Functional Assessment of Cancer Therapy/Gynecologic Oncology Group-Neurotoxicity-12 (FACT/GOG-Ntx-12) Version 4. The Ntx-12 contains 12 items, each on a five-point Likert scale (total range: 0-48), where higher scores indicated more severe symptoms. In the present study, the Ntx-12 had Cronbach's α reliabilities of .86 and .89, respectively, at two time points of assessment [21]. In this study, we calculated the difference between NTx-12 scores evaluated immediately before chemotherapy initiation and at the end of 2nd chemotherapy cycle. A positive value indicated that CIPN symptoms had occurred, and the magnitude of the value indicated the severity of the symptoms. Likewise, we calculated the difference between NTx-12 scores evaluated at the end of the 2nd and 4th (or 3rd) chemotherapy cycles to determine changes in CIPN symptoms (possible range: -48 to 48). Positive values indicated aggravated symptoms, and negative values indicated symptom relief; the magnitude of the score change indicated the

https://doi.org/10.7586/jkbns.2022.24.2.86

degree of change in the symptoms.

- *Non-pharmacologic factors*: Participants were asked whether they applied exercise (walking, hiking, gardening), massage (foot, body), and heat therapy (foot baths, tub baths) to relieve CIPN symptoms, and how many times per week they performed each therapy. Unlike hiking or gardening, the number of participants that reported walking was sufficient to perform statistical analyses of subgroups based on the weekly frequency of walking.
- *Psychosocial factors*: In this study, we measured social support, depression, and anxiety as psychosocial factors that could affect the perception of CIPN symptoms. Social support was assessed with the Medical Outcomes Study Social Support Survey (MOS-SSS) [22]. Total score ranged from 0 to 100, where a higher the score indicated higher perceived social support. In the present study, the Cronbach's α was .98, at two time points of assessment . Depression and anxiety were measured with the Hospital Anxiety and Depression Scale (HADS). The HADS consists of a seven-item depression scale (HAD-D) and a seven-item anxiety scale (HAD-A), rated on 4-point Likert scales (range: 0 to 21 points each). Higher scores indicated higher levels of depression and anxiety [23]. In the current study, the internal reliabilities of HADS-D and HADS-A were .80 and .79, respectively, at the end of the 2nd chemotherapy cycle; and .84 and .84, respectively, immediately before the last chemotherapy cycle.

4. Data collection

This study was approved by the K University Medical Center Institutional Review Board (IRB No. 0343-055). All eligible patients were informed on study participation in detail, and then data were gathered with interviews and retrieved from medical records of subjects that provided written informed consent. In this short-term prospective study, data were collected by the investigator and a research assistant. Demographic data, disease and chemotherapy related data were rerieved from medical records. Three face-to-face interviews per participant were conducted when the participants visited the hospital to start the 1st, 3rd and the last chemotherapy cycles. That is, immediately before the initiation of chemotherapy and at the end of the 2nd and 4th (or 3rd) chemotherapy cycles. The timing of the two assessments conducted after initiating antineoplastic drug administration were determined based on previous studies, which showed that CIPN symptoms occurred with mean cumulative doses of 300 mg/m^2 for cisplatin and 400 mg/m^2 for docetaxel [9,24]. The total number of required chemotherapy cycles was based on the dose of chemotherapeutic agent. For example, patients with breast cancer that were treated with the docetaxel and cyclophosphamide combination therapy completed treatment after the 4th chemotherapy cycle. Therefore, the final data collection for those patients was at the end of the 3rd chemotherapy cycle. The data collection period was from August 10, 2018 to July 23, 2019.

5. Data Analysis

We applied the t-test, ANOVA, or Pearson correlation analysis to investigate associations between CIPN symptom changes and independent variables. Factors that showed a significant association ($p < .100$) in the univariate analysis were entered as independent variables in the multivariate analysis (multiple regression analysis). Statistical Package for the Social Sciences (SPSS) version 25.0 was used for statistical analyses.

RESULTS

1. Participant characteristics

Participant demographic and disease-related characteristics are shown in Table 1. Among the 130 patients, 23 (17.7%) had gastric cancer, 79 (60.8%) had colorectal cancer, and 28 (21.5%) had breast cancer. At the time of diagnosis, 33 patients (25.4%) had stage 1 or 2 cancer, and 97 patients (74.6%) had stage 3 or 4 cancer. The time interval between surgery and the initiation of chemotherapy was less than 1 month in 71 patients (54.6%). Twenty-eight patients (21.5%) received a taxane-based (Docetaxel) combination therapy, and the remaining participants (78.5%) received platinum-based (Oxalipatin) combination therapy.

Prior to the start of chemotherapy, 75 patients (57.7%) had no symptoms (0 points), and 37 patients (28.5%) scored only 1 or 2 points in the CIPN symptom scores (Table 1). Table 2 shows the incidence and changes in CIPN symptoms. A CIPN occurrence was defined as a score above the baseline score. At the end the 2nd chemotherapy cycle, 121 patients (93.1%) had CIPN symptoms, and score increases of 1 to 10 were reported by 43.9% of subjects. At the end of the 4th chemotherapy cycle (or the 3rd cycle in the patients with breast cancer), CIPN symptoms were aggravated compared to the score at the end of the 2nd chemotherapy cycle in 39.2% of patients and alleviated in 50.8% of patients. NTx-12 scores increased or decreased by less than 10 points in 33.0% and 43.1% of pa-

 https://doi.org/10.7586/jkbns.2022.24.2.86

Table 1. Characteristics of Study Participants (N = 130)

Variables	N (%)
Gender	
Female	59 (45.4)
Male	71 (54.6)
Age (yr)	
Mean ± SD	57.2 ± 9.7
Yonger than 55	51 (39.2)
55-64	55 (42.3)
65 and older	24 (18.5)
Marital status	
Single	9 (6.9)
Married	103 (79.2)
Divorced/Separated/Bereavement	18 (13.9)
Occupational status (Before chemotherapy)	
Unemployed	34 (26.2)
Employed	96 (73.8)
Diagnosis	
Stomach cancer	23 (17.7)
Colorectal cancer	79 (60.8)
Breast cancer	28 (21.5)
Cancer stage	
Stage I, II	33 (25.4)
Stage III, IV	97 (74.6)
Period since surgery (month)	
< 1	71 (54.6)
≥ 1	59 (45.4)
Chemotherapeutic agents	
Taxane group (Docetaxel based combination therapy)	28 (21.5)
Platinum group (Oxaliplatin based combination therapy)	102 (78.5)
Score of CIPN before chemotherapy	
0	75 (57.7)
1-2	37 (28.5)
3-8	18 (13.8)

SD = Standard deviation; CIPN = Chemotherapy induced peripheral neuropathy.

tients, respectively.

2. Associations between CIPN symptoms and potential influencing factors

The t-test and ANOVA results are shown in Table 3. The type of anticancer drug, the use of pain medication and the performance of gardening were not significantly associated with changes in CIPN symptoms. CIPN symptom relief was significantly associated with walking (F = -6.24, p = .003), hiking (t = 2.53, p = .013), massage (t = 2.24, p = .027), and heat therapy (t = 2.34, p = .021) during the time between chemotherapy initiation and the end of the 2nd chemotherapy cycle. During the time between the end of the 2nd and the end of the 4th (or 3rd) chemotherapy cycles, CIPN symptom relief was significantly associated with walking (F = -18.10, p < .001), hiking (t = 3.64, p < .001), massage (t = 4.88 p < .001), and heat therapy (t = 5.73, p < .001).

Table 2. Occurrence and Change of Chemotherapy Induced Peripheral Neuropathy (N = 130)

Variables		n (%)
Occurrence† of CIPN		
No		9 (6.9)
Yes		
Severity of CIPN	1-10	57 (43.9)
	11-20	52 (40.0)
	21-30	12 (9.2)
	Total (10.58 ± 7.25)	121 (93.1)
Change‡ of CIPN		
Aggravated		
Degree of aggravation	11-21	8 (6.2)
	1-10	43 (33.0)
	Total (6.24 ± 4.50)	51 (39.2)
No change		13 (10.0)
Alleviated		
Degree of alleviation	-1~-10	56 (43.1)
	-11~-23	10 (7.7)
	Total (-6.49 ± 4.90)	66 (50.8)

†Score change at the end of 2nd chemotherapy cycle from baseline; ‡Score change at the end of 3rd/4th chemotherapy cycle from the end of the 2nd cycle.
CIPN = Chemotherapy induced peripheral neuropathy.

As a results of correlation analysis (Table 4), at the end of the 2nd chemotherapy cycle, CIPN symptom changes were not significantly correlated with perceived social support, depression, or anxiety. However, during the interval between the end of the 3rd and 4th chemotherapy cycles, CIPN symptom changes were significantly correlated with social support, depression, and perceived anxiety (coefficients (r): -.17, p = .048; .31, p < .001; and .18, p = .036, respectively).

3. Factors that influence changes in CIPN symptoms

The correlation coefficients for anxiety and depression in two times of measure were .73 and .74, respectively; due to this multicolinearity, we excluded anxiety from the independent variables of multiple regression analysis [25]. The other independent variables showed no multicollinearity; the variance inflation factors were less than 10 (1.37-2.88), and the tolerances were above .10 (.35-.73) [26]. In addition, based on the inclusion of 12 independent variables, 130 cases, and α = .05 in this study, the Durbin-Watson statistic (d) was expected to be between 1.53 and 1.80. Our results (d = 1.90) showed no autocorrelations in residuals; therefore, the assumptions required for a multiple regression analysis were satisfied [26]. The regression analysis (Table 5) showed that the regression model was significant (F = -7.54, p = < .001), and the R^2 was .44.

The most influential factor in alleviating CIPN symptoms was heat

https://doi.org/10.7586/jkbns.2022.24.2.86

therapy during the 3rd and 4th chemotherapy cycle (β = -.34, p < .001). Other significant protective factors for CIPN symptoms were massage therapy during the 3rd and 4th chemotherapy cycle (β = -.21, p = .012) and walking 5 times or more per week, performed during the 1st and 2nd chemotherapy cycle (β = -.26, p = .021). Conversely, recently perceived depression had a significant negative effect on CIPN symptoms (β = .19, p = .027). In other words, depression made CIPN symptoms worse.

Table 3. The Association between Physical or Behavioral Variables and Change of CIPN (N = 130)

Time frame	Variables	n	Change of CIPN (Mean ± SD)	t or F	p
The 1st and 2nd chemotherapy cycle	Chemotherapeutic agents				
	Taxane†	28	11.75 ± 4.24	-0.93	.336
	Platinum‡	102	10.25 ± 7.86		
	Pain medication for CIPN				
	No	106	-1.14 ± 7.66	-0.95	.347
	Yes	24	0.46 ± 6.71		
	Exercise				
	Walking				
	No	28	1.89 ± 8.37	-6.24	.003
	1-4 times/week	49	0.41 ± 7.60		
	≥ 5 times/week	53	-3.45 ± 6.08		
	Hiking				
	No	114	-0.24 ± 7.59	2.53	.013
	Yes	16	-5.19 ± 5.01		
	Gardening				
	No	119	-0.93 ± 7.54	-0.43	.666
	Yes	11	0.09 ± 7.18		
	Massage (Foot or body massage)				
	No	110	-0.23 ± 7.63	2.24	.027
	Yes	20	-4.25 ± 5.72		
	Heat therapy (Foot or tub bath)				
	No	114	-0.28 ± 7.43	2.34	.021
	Yes	16	-4.88 ± 6.82		
The 3rd and 4th chemotherapy cycle§	Chemotherapeutic agents				
	Taxane†	28	0.89 ± 7.63	-1.94	.166
	Platinum‡	102	-1.32 ± 7.42		
	Pain medication for CIPN				
	No	105	-1.10 ± 7.68	-0.81	.422
	Yes	25	0.24 ± 6.65		
	Exercise				
	Walking				
	No	29	1.00 ± 6.23	-18.10	< .001
	1-4 times/week	53	2.26 ± 7.29		
	≥ 5 times/week	48	-5.40 ± 6.157		
	Hiking				
	No	108	0.19 ± 7.52	3.64	< .001
	Yes	22	-5.91 ± 4.91		
	Gardening				
	No	118	-0.60 ± 7.54	1.17	.245
	Yes	12	-3.25 ± 6.84		
	Massage (Foot or body massage)				
	No	92	1.05 ± 6.96	4.88	< .001
	Yes	38	-5.45 ± 6.77		
	Heat therapy (Foot or tub bath)				
	No	95	1.20 ± 6.81	5.73	< .001
	Yes	35	-6.40 ± 6.42		

†Docetaxel based combination therapy; ‡Oxaliplatin based combination therapy; §During the only 3rd chemotherapy cycle among participants with breast cancer (n = 28).
SD = Standard deviation; CIPN = Chemotherapy induced peripheral neuropathy.

 https://doi.org/10.7586/jkbns.2022.24.2.86

DISCUSSION

Our CIPN incidence rate (93.1%) was higher than those observed in previous studies. A previous systematic review [5] reported an incidence rate of 68.1% within 4 weeks of the end of chemotherapy. We speculated that our high CIPN incidence compared to a previous study was probably due to different time point of measure and different type of anticancer drug. In our study, 78.5% of the participants received oxaliplatin which cause acute neuropathy after immediately after infusion [27]. About a half participants in the current study showed score changes of 10 points or less, out of a possible 48 points, which indicated that their symptoms were not very serious. This finding was similar to the results of a previous study [20], which reported that about 40% of cases showed a grade I CIPN symptom severity (asymptomatic or paresthesia or mild motor symptoms), measured with the Common Terminology Criteria for Adverse Events. The mild symptom severity we observed might have been related to the fact that this study only included subjects that received docetaxel, which is known to have relatively little neurotoxicity among the family of taxanes [20]. However, in the current study, the CIPN symptoms were measured with the Ntx-12, which did not provide a cut-off score for distinguishing symptom severity. Therefore, the results should be interpreted with caution.

Regular heat therapy (footbath or tub-bath) performed during the recent 4-6 weeks was the most influential factor in alleviating CIPN symptoms. Another factor that can significantly decrease CIPN symptoms is massage (foot or body) performed regularly between the 3rd and the 4th chemotherapy cycles. Heat and massage increase blood circulation, which prevents the accumulation of irritants [28]; thus, these can maintain normal autonomic nervous system activity and control pain. A meta-analysis on non-pharmacological interventions, including footbaths and massage, confirmed these effects on CIPN symptoms [17]. That meta-analysis included studies on the effects of massage and footbaths provided by a nurse or therapist. The results of the current study are thought to be meaningful, because the effects of heat therapy and massage applied by patients or family members at home were identified. In adiition, we found that, the effects of heat therapy and massage on relief of CIPN symptoms did not last long. That finding might be explained by the fact that heat therapy and massage are symptomatic treatments, which cannot restore nerve cells. Similarly, the previous meta-analysis showed that more frequent applications of heat or massage per

Table 4. Correlation between Psychological Variables and Change of CIPN (N = 130)

Variables	Change of CIPN r (*p*)	
	The 1st and 2nd chemotherapy cycle	The 3rd and 4th chemotherapy cycle†
Social support	-.10 (.241)	-.17 (.048)
Depression	.08 (.367)	.31 (< .001)
Anxiety	.01 (.871)	.18 (.036)

†During the only 3rd chemotherapy cycle among participants with breast cancer (n = 28).
CIPN = Chemotherapy induced peripheral neuropathy.

Table 5. Results of Linear Regression Analyis on Change of Chemotherapy Induced Peripheral Neuropathy (N = 130)

Time frame	Variables	B	SE	β	t	*p*
The 1st and 2nd chemotherapy cycle	Constant	0.70	2.57		0.27	.786
	Exercise					
	Walking, 1-4 times/week	-1.78	1.59	-.12	-1.22	.264
	Walking, ≥ 5 times/week	-3.94	1.69	-.26	-2.33	.021
	Hiking	-0.54	1.99	-.02	-0.27	.786
	Massage (Foot or body massage)	1.58	1.71	.09	1.05	.294
	Heat therapy (Foot or tub bath)	1.34	1.90	.07	0.83	.407
The 3rd and 4th chemotherapy cycle†	Exercise					
	Walking, 1-4 times/week	1.83	1.55	.12	1.18	.240
	Walking, ≥ 5 times/week	-0.94	1.82	-.06	-0.52	.606
	Hiking	-2.69	1.76	-.14	-1.53	.129
	Massage (Foot or body massage)	-3.49	1.38	-.21	-2.54	.012
	Heat therapy (Foot or tub bath)	-5.37	1.56	-.34	-3.67	< .001
	Social support	0.02	0.03	.05	0.61	.545
	Depression	0.39	0.18	.19	2.24	.027

$R^2 = .44$, $F = -7.54$, $p < .001$.

†During the only 3rd chemotherapy cycle among participants with breast cancer (n = 28).

https://doi.org/10.7586/jkbns.2022.24.2.86

week had a larger effect size than long periods of intervention [17].

This analysis indicated that walking 5 times or more per week during the interval between chemotherapy initiation and the end of the 2nd chemotherapy cycle (for 6 weeks) had a significant effect on CIPN symptom relief. However, CIPN symptoms were not significantly alleviated by walking less than 5 times per week in any period or by walking during the 4-6 weeks after the initiation of 3rd chemotherapy cycle. To reduce CIPN symptoms, it was suggested that patients should walk regularly more than 4 times per week, for more than 6 weeks. The importance of walking was demonstrated in a previous study, which showed that exercise for more than 150 minutes per week (≥ 3 MET) reduced CIPN symptoms in patients with colorectal cancer [11]. Indeed, exercise can induce the recovery of axons and myelin by promoting energy production in the mitochondria and increasing blood supply to peripheral nerves [11,29]. However, it takes time for nerves to regenerate. Consequently, it might be more relevant to measure the effects of walking at least 6 weeks after the patient starts walking.

Among the psychosocial factors tested, only depression, measured at the end of the 4th chemotherapy cycle (or the 3rd cycle in participants with breast cancer), worsened CIPN symptoms. This result was consistent with a previous study [19] that showed that depression had the largest effect on CIPN symptoms among 140 patients with colorectal cancer that received oxaliplatin. They showed that depression had a stronger effect than anxiety and social support. However, we found that depression measured at the end of the 2nd chemotherapy cycle did not affect the CIPN symptoms. This result might be explained by the fact that the psychological state can readily change over time. In addition, it might be unclear whether the psychological state affected the CIPN symptoms, or vice versa.

Although a high proportion of subjects perceived CIPN symptoms, the rate of analgesic prescriptions was low, and the use of pain medication was not correlated to CIPN symptom relief. This finding was consistent with the treatment guidelines for CIPN, which do not recommend pain medication, except for duloxetine [10]. The low frequency of drug prescriptions might be explained by the low severity of CIPN symptoms in these participants, the lower priority of dealing with CIPN symptoms compared to treating cancer, and the passive attitude toward CIPN symptoms [30]. Indeed, compared to patients, physicians commonly under-report the incidence and severity of CIPN symptoms [9]. Consequently, it is necessary for nurses to provide CIPN-related training at the initiation of chemotherapy to facilitate timely consultations between cancer survivors and the medical staff to ensure that appropriate interventions are administered to alleviate CIPN symptoms. In other words, it is essential that both the medical staff and the patients are sufficiently informed to overcome issues of underdiagnosis and underassessment.

The current study was limited, due to the small number of subjects that applied non-pharmacologic interventions; therefore, it was not possible to analyze CIPN symptom relief according to the their frequency. In addition, although this study applied a prospective design, the temporal relationship between depression and CIPN symptoms was not clear. We thought that longitudinal studies involving a larger number of participants are needed to correct the mentioned limitations.

CONCLUSION

This study showed that most patients (93.1%) that received postoperative docetaxel or oxaliplatin as an adjuvant chemotherapy developed CIPN symptoms at the end of the 2nd chemotherapy cycle. We showed that walking 5 or more times per week for 6 weeks could alleviate CIPN symptoms. Additionally, regular heat therapy or massages for 4-6 weeks could relieve CIPN symptoms. However, depression had a negative effect on symptom relief. Based on these results, we suggested that a comprehensive management program is needed, which includes walking, heat therapy, massages, and mood therapy to relieve CIPN symptoms in patients that survive cancer.

CONFLICTS OF INTEREST

The authors declared no conflict of interest.

AUTHORSHIP

GSJ and HC contributed to the conception and design of this study; GSJ collected data; GSJ and HC performed the statistical analysis and interpretation; GSJ, HC, and JYC drafted the manuscript; HC and JYC critically revised the manuscript; HC supervised the whole study process. All authors read and approved the final manuscript.

https://doi.org/10.7586/jkbns.2022.24.2.86

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