RESEARCH BRIEF

Exploring Analgesic Use Patterns Among Cancer Survivors With Chronic Chemotherapy-Induced Peripheral Neuropathy

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OBJECTIVES: To explore cancer survivors' historical and current use of analgesics for chronic chemotherapy-induced peripheral neuropathy (CIPN).

SAMPLE & SETTING: 142 post-treatment cancer survivors who received neurotoxic chemotherapy and were experiencing moderate to severe CIPN.

METHODS & VARIABLES: Participants completed the Treatment-Induced Neuropathy Assessment Scale at baseline and reported all analgesics used to manage CIPN. Frequency of historical or current prescription analgesic use for chronic CIPN was described and stratified by CIPN pain severity.

RESULTS: At baseline, 31% of participants reported historical use of analgesics for CIPN and 46% of participants were currently using analgesics for CIPN. Gabapentin was the most frequently used analgesic, historically (20%) and currently (34%), and duloxetine was used less frequently (6% historical use, 10% current use). Many participants with severe pain (59%) reported using analgesics for CIPN.

IMPLICATIONS FOR NURSING: Duloxetine, the first-line treatment for chronic CIPN pain, was used less frequently than gabapentin, a common prescription analgesic for neuropathic pain. Further research is needed to determine strategies to promote the implementation of evidence-based CIPN treatments in clinical practice.

KEYWORDS analgesics; chemotherapy-induced peripheral neuropathy; cancer pain

***ONF, 51*(5), 445–450.**

DOI 10.1188/24.ONF.445-450

Chemotherapy-induced peripheral neuropathy (CIPN) is a side effect of neurotoxic chemotherapy administration (e.g., taxanes, vinca alkaloids) and persists chronically after treatment completion in about 60% of patients (Seretny et al., 2014). Chronic CIPN (bilateral numbness, tingling, neuropathic pain, and/or weakness) negatively affects individuals' ability to carry out activities of daily living (Gewandter et al., 2013; Knoerl, Mazzola, et al., 2022) and increases fall risk (Winters-Stone et al., 2017). Only one guideline-based treatment is recommended for painful CIPN (i.e., duloxetine), and there are no guideline-based treatments available for nonpainful CIPN or CIPN-related functional deficits (Loprinzi et al., 2020).

Various factors may influence clinicians' decisions regarding which treatments to prescribe for CIPN in clinical practice, including patients' concerns about additional side effects from medication, insurance barriers, drug–drug interactions (Knoerl et al., 2023), and lack of clinician knowledge surrounding available CIPN treatments (Tanay et al., 2022). As such, several analgesic medications are currently prescribed in clinical practice for CIPN management. For example, claims data suggest that within the first six months of initiating neurotoxic chemotherapy, gabapentin, pregabalin, and duloxetine were dispensed to approximately 7%, 1%, and 1% of patients, respectively (Gewandter et al., 2020). These data are limited because it is not known what percentage of these patients developed CIPN from the neurotoxic chemotherapy or for what these analgesics were prescribed, but they suggest that duloxetine may be underutilized to treat CIPN. The purpose of this secondary analysis is to explore cancer survivors' self-reported historical and current use of prescription analgesics for the

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treatment of chronic CIPN. Identifying patterns in analgesic use among cancer survivors with chronic CIPN may reveal important gaps in survivorship care that can be targeted by future interventions (e.g., education to clinicians) and types of prescription analgesic medications that may positively affect CIPN in clinical practice settings.

TABLE 1. Sample Characteristics (N = 142)

Characteristic	$\bar{X}$	SD
Age at consent (years)	62.9	9.6
Characteristic	**n**	**%**
Sex		
Female	92	65
Male	50	35
Ethnicity		
Hispanic	2	1
Non-Hispanic	133	94
Choose not to answer	2	1
Unknown	5	4
Race		
American Indian or Alaska Native	1	1
Black or African American	15	11
White	120	85
More than 1 race	4	3
Choose not to answer	2	1
Cancer diagnosis		
Breast	51	36
Gastrointestinal	49	35
Hematologic	14	10
Gynecologic	13	9
Other	15	11
Neurotoxic chemotherapy		
Platinum only	53	57
Taxane only	52	37
Platinum and taxane	23	16
Bortezomib only	7	5
Vinca alkaloid only	7	5
TNAS worst CIPN score		
No pain (0)	28	20
Mild pain (1–3)	24	17
Moderate pain (4–6)	32	23
Severe pain (7–10)	58	41

CIPN—chemotherapy-induced peripheral neuropathy; TNAS—Treatment-Induced Neuropathy Assessment Scale
Note. Additional details regarding the sample characteristics are described along with the primary results of the randomized controlled trial (Gewandter et al., 2024).
Note. Because of rounding, percentages may not total 100.

Methods

Design, Sample, and Setting

The following reports a secondary analysis of baseline data collected as part of a phase 2 clinical trial that aimed to determine the efficacy of a wireless transcutaneous electrical nerve stimulation device for chronic CIPN (N = 142) (NCT04367490, April 29, 2020) (Gewandter et al., 2024). Participants were eligible if they were adults; had completed treatment with a platinum, a taxane, a vinca alkaloid, or bortezomib at least three months prior to screening; had been diagnosed with CIPN by their clinician; and had reported a severity score of 4 or greater on the Treatment-Induced Neuropathy Assessment Scale (TNAS) for at least two of the following symptoms in the bilateral lower extremities: worst hot/burning pain, sharp/shooting pain, tingling, numbness, or cramping. Participants were recruited from six National Cancer Institute Community Oncology Research Program sites associated with the University of Rochester Cancer Center National Cancer Institute Community Oncology Research Program Research Base. Study oversight was provided by the National Cancer Institute Central Institutional Review Board, and all participants provided written informed consent.

Data Collection

Prior to the study intervention (at study baseline), participants completed the TNAS (Mendoza et al., 2015) item pertaining to the worst pain experienced in the arms, legs, hands, or feet in the past 24 hours (scored from 0 to 10, with higher scores representing worse pain) and a standardized demographic questionnaire. There is evidence supporting the test–retest reliability (intraclass correlation coefficient = 0.97) and concurrent validity of the TNAS (r = 0.69 between the TNAS and the European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire–Chemotherapy-Induced Peripheral Neuropathy 20 sensory subscale) (Mendoza et al., 2015). Participants listed all analgesics and treatments historically or currently used to manage CIPN. All questionnaires were administered in person at the study visit. Study staff abstracted the following information from participants' electronic health records: (a) neurotoxic cancer therapy type and dose, (b) time since last neurotoxic cancer treatment, (c) cancer

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type, (d) current analgesics, and (e) past medical conditions.

Statistical Analysis

The frequency of the type of prescription analgesics participants had historically used (i.e., any use of analgesics for CIPN in the past) or were currently using to treat CIPN was summarized. The frequency of participants' historical or current use of prescription analgesics to treat CIPN was stratified by TNAS worst pain category scores (no pain = 0, mild pain = 1–3, moderate pain = 4–6, severe pain = 7–10).

Results

Participant Characteristics

Table 1 describes the demographic characteristics of the enrolled sample (N = 142). Of the entire sample, 20% (n = 28) reported no pain, 17% (n = 24) reported mild pain, 23% (n = 32) reported moderate pain, and 41% (n = 58) reported severe pain on the TNAS 0–10 numeric rating scale of worst CIPN pain intensity.

Frequency of Historical and Current Prescription Analgesic Use for CIPN

Table 2 describes the frequency of participants' historical and current use of prescription analgesics for CIPN. At baseline, 31% (n = 44) of participants reported having previously used prescription analgesics for CIPN, and 46% (n = 66) of participants were currently using prescription analgesics. Gabapentin was the most frequent historical (n = 29, 20%) and current prescription analgesic (n = 48, 34%) used for the treatment of CIPN, followed by opioids (6% [n = 8] historical use, 11% [n = 15] current use) and duloxetine (6% [n = 8] historical use, 10% [n = 14] current use). Among participants currently using opioids (N = 15), 11 participants (73%) had previously tried other analgesics (e.g., 2 had previously tried duloxetine). In addition, among participants currently using duloxetine (N = 14), 3 (21%) had previously tried opioids and 1 had tried gabapentin for CIPN pain. Of the 142 study participants, 13 (9%) reported previous use of at least two analgesics, and 18 participants (13%) reported using more than one analgesic currently. As for over-the-counter prescription analgesics, 5 (4%) were currently using acetaminophen and 13 (9%) were using nonsteroidal anti-inflammatory agents for CIPN.

Discussion

This study's findings highlighted the frequency of prescription analgesic use among cancer survivors with chronic CIPN. Close to one-third of participants in the study were currently using gabapentin for the treatment of chronic CIPN. These data are consistent with a prior report on patients currently receiving neurotoxic chemotherapy by Gewandter et al. (2020), which found that gabapentin was prescribed more commonly than pregabalin or duloxetine even though duloxetine is the only evidence-based therapy for CIPN that is recommended by the American Society of Clinical Oncology (Loprinzi et al., 2020). The high rate of gabapentin prescription is largely unsurprising because clinicians may be more familiar with gabapentin than other analgesics as a treatment modality for chronic CIPN (Knoerl et al., 2023).

Given the risks of opioids (e.g., overdose, misuse), they are recommended as a last resort for chronic pain (Dowell et al., 2022). About 11% (n = 15) of participants reported currently taking opioids for chronic CIPN management, and 27% (n = 4) of those participants did not report trying any other medications prior to starting opioid treatment. These data suggest a potential necessity for physicians to reevaluate the order in which they prescribe different analgesics for CIPN. Of note, treatment with opioids prior to other neuropathic pain medications could occur because of potential contraindications for the preferred treatments.

Although 46% of the sample was currently using prescription analgesics for the management of chronic CIPN pain, the majority of participants were still experiencing moderate to severe CIPN pain. This level of prescription analgesic use highlights the unmet need of these patients. At the same time, 54% of the sample was not using prescription analgesics, potentially indicating cancer survivors' interest in nonpharmacologic treatments for CIPN (Knoerl, Berry, et al., 2022). Taken together, these

KNOWLEDGE TRANSLATION

- Cancer survivors with chronic chemotherapy-induced peripheral neuropathy (CIPN) pain infrequently reported taking evidence-based treatments for CIPN pain; about 17% (n = 15) of cancer survivors with moderate or greater CIPN pain reported previously and/or currently using duloxetine, the recommended first-line treatment for CIPN pain.
- Cancer survivors reported high rates of CIPN pain despite analgesic use; about 59% (n = 34) of participants with severe CIPN pain reported using analgesics.
- Further research is needed to develop strategies directed toward clinicians to increase the prescription of evidence-based treatments among cancer survivors with chronic CIPN.

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findings highlight the need for further research to determine the efficacy of novel analgesics and nonpharmacologic treatments for chronic CIPN. Of the nonpharmacologic treatments, exercise interventions have the largest evidence base for efficacy in CIPN management (Tamburin et al., 2022), but they are not currently recommended by clinical practice guidelines (Loprinzi et al., 2020).

Limitations

There are several limitations to the research. First, these data are based on a convenience sample and are not generalizable to all patients with CIPN. In addition, the reported frequencies of previous or current prescription analgesic use for chronic CIPN pain do not reflect the possibility that participants who were offered prescription medications declined because

TABLE 2. Frequency of Cancer Survivors' Historical and Current Use of Analgesics, Stratified by Chemotherapy-Induced Peripheral Neuropathy Pain Severity at Baseline

	Overall (N = 142)		No Pain (N = 28)		Mild Pain (N = 24)		Moderate Pain (N = 32)		Severe Pain (N = 58)	
Analgesic	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Historical prescription analgesics										
Gabapentin	29	20	5	18	5	21	5	16	14	24
Pregabalin	8	6	1	4	2	8	1	3	4	7
Duloxetine	8	6	1	4	2	8	–	–	5	9
Opioid	8	6	1	4	–	–	3	9	4	7
Venlafaxine	6	4	–	–	2	8	–	–	4	7
Amitriptyline	2	1	–	–	1	4	–	–	1	2
Steroid	1	1	–	–	–	–	–	–	1	2
Multiple	13	9	1	4	2	8	1	3	9	16
None	98	69	21	75	15	63	24	75	38	66
Current prescription analgesics										
Gabapentin	48	34	7	5	8	33	8	25	25	43
Opioid	15	11	–	–	3	13	2	6	10	17
Duloxetine	14	10	1	4	3	13	4	13	6	10
Pregabalin	4	3	–	–	1	4	1	3	2	3
Venlafaxine	2	1	–	–	–	–	1	3	1	2
Amitriptyline	1	1	–	–	–	–	1	3	–	–
Steroid	1	1	–	–	–	–	–	–	1	2
Multiple	18	13	–	–	5	21	3	10	10	17
None	76	54	20	71	14	58	18	56	24	41

Note. Percentages in each column reflect the frequency at which participants reported use of each specific analgesic, multiple analgesics, or no analgesic out of the total number of participants specified in the column header (i.e., pain intensity category). The frequencies total greater than 100% for each column because participants who were taking more than 1 prescription analgesic were counted under the multiple analgesic category as well under each applicable analgesic category.

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of concern about side effects or for other reasons. Finally, there is the possibility of recall bias because historical prescription analgesic use was self-reported by participants.

Implications for Nursing

Although 63% (n = 90) of cancer survivors with chronic CIPN were experiencing moderate or greater CIPN pain intensity, only 17% (n = 15) of cancer survivors with moderate or greater CIPN pain intensity had previously used or were currently using duloxetine, the first-line treatment for CIPN pain (Loprinzi et al., 2020). Qualitative evidence suggests that a barrier to duloxetine prescription is that insurance companies may require participants to try and fail gabapentin first (Knoerl et al., 2023). However, among the current duloxetine users in this study (n = 14, 10%), only one participant had previously tried gabapentin for CIPN pain management, suggesting that previous gabapentin use was generally not a requirement for duloxetine use in this sample. Clinicians also report hesitancy to prescribe duloxetine to patients receiving other antidepressants because of drug–drug interactions (Knoerl et al., 2023), which may account for the observed higher rates of gabapentin versus duloxetine use. Other data demonstrate that duloxetine has a better side effect profile compared with gabapentin in the treatment of diabetic peripheral neuropathic pain (Jiang et al., 2022). However, further research is needed to identify cancer survivors with CIPN pain and increase the uptake of evidence-based treatments for chronic CIPN in clinical practice. Prior studies have evaluated electronic care planning software or algorithms that have incorporated patient-reported CIPN outcomes and recommendations for CIPN management, but such interventions have not been shown to significantly increase the prescription of duloxetine for CIPN pain (Knoerl et al., 2018, 2021).

Conclusion

The study results demonstrate that cancer survivors with chronic CIPN pain (a) infrequently report taking evidence-based treatment (i.e., duloxetine) for CIPN pain and (b) still experience higher rates of CIPN pain despite analgesic use. Further research is needed to develop strategies to increase the uptake of evidence-based CIPN treatment (e.g., increase clinician knowledge regarding recommended use of duloxetine for chronic CIPN), improve the identification of CIPN pain in practice, and identify novel treatments for CIPN.

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(Submitted December 2023. Accepted February 23, 2024.)

This research was funded, in part, by a grant from the National Institute for Neurologic Disorders and Stroke (K24NS126861) and grants from the National Cancer Institute (R21CA235389 and UG1CA189961).

Knoerl, Morrow, Mustian, Gauthier, and Gewandter contributed to the conceptualization and design. Francar, O'Rourke, Mustian, and Gewandter completed the data collection. Sohn provided statistical support. Sohn and Gewandter provided the analysis. Knoerl, Sohn, Foust, Morrow, Mustian, Gauthier, and Gewandter contributed to the manuscript preparation.

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