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Review Article

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An Integrative Review of the Effectiveness of Duloxetine Use in Cancer Patients Receiving Chemotherapy

Cheryl Adair*, Kelly Beavers, Martha Cardenas, Felicia Croft and Courtney Rich

College of Nursing, Northwestern State University, Shreveport, Louisiana, USA

***Corresponding author**
Cheryl Adair, College of Nursing, Northwestern State University, Shreveport, Louisiana, USA.

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ABSTRACT

Purpose: The objective of this Integrative Review of Literature (IRL) was to assess the efficacy of duloxetine in the management of chemotherapy-induced peripheral neuropathy (CIPN) among cancer patients. Peripheral neuropathy associated with chemotherapy manifests as symptoms such as tingling, burning, numbness, weakness, or pain in the hands and feet. The detrimental and, in some cases, debilitating impact of CIPN on individuals undergoing cancer treatment underscores the significance of investigating the effectiveness of duloxetine as part of the treatment plan for this condition.

Procedure: A comprehensive literature search was performed to identify peer-reviewed journal articles on the effectiveness and safety of the use of duloxetine for the treatment of CIPN. The search was conducted using two electronic databases: CINHAL and PubMed. Additional supplemental sources, including the American Cancer Society, American Society of Clinical Oncology, Google Scholar, and Medline, were used to compile additional information for review.

Results: The strengths and weaknesses of each article were reviewed utilizing the Johns Hopkins Research Appraisal tool. A data synthesis review exhibited good to high-quality articles with a range of evidence, including Level I, Level II, and Level III. Research yielded positive outcomes in reducing pain, increasing quality of life, and reducing the severity of symptoms for both physical and mental health with Duloxetine treatment. Results showed effectiveness and tolerability in the treatment of CIPN. Adding Duloxetine to the CIPN treatment plan positively impacted pain management and enhanced quality of life (QoL).

Conclusion: Studies revealed that Duloxetine, as a pharmacologic intervention, resulted in a reduction in pain and an improvement in the quality of life (QoL) for patients experiencing chemotherapy-induced peripheral neuropathy (CIPN). Duloxetine demonstrated enhanced effectiveness, safety, and tolerability in its outcomes. Notably, the American Society of Clinical Oncology has designated Duloxetine as the standard of care for CIPN. Given its status as the standard of care, there is a higher likelihood of favorable considerations for Duloxetine by insurance companies.

Keywords: Chemotherapy-Induced Peripheral Neuropathy, Duloxetine

Introduction

Peripheral neuropathy is a set of symptoms caused by damage to the nerves outside the brain and spinal cord. Patients suffering from peripheral neuropathy may notice tingling, burning, numbness, weakness, or pain in the hands and feet. Some chemotherapy and other drugs used to treat cancer can damage peripheral nerves, resulting in chemotherapy-induced peripheral neuropathy (CIPN) [1]. CIPN is a significant and, in some cases, debilitating adverse effect of cancer treatment in some patients.

There is no known cure for CIPN, and it creates challenges through treatment as CIPN impacts quality of life and adherence. Duloxetine is a serotonin-norepinephrine reuptake inhibitor that has emerged as a viable potential therapeutic option for alleviating CIPN symptoms. CIPN-related symptoms often persist for more than six months after cessation of chemotherapy [2].

This integrative review of literature sought to synthesize current research findings from multiple disciplines to determine the efficacy of duloxetine for treating chemotherapy-induced peripheral neuropathy (CIPN) among past or present chemotherapy patients. This integrative review meticulously evaluated the methodologies employed in the studies, providing a thorough, comprehensive analysis of the evidence substantiating the efficacy of duloxetine in CIPN management. Furthermore, the objective of this team was to identify potential research gaps, suggest avenues for further investigation, and propose

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avenues for future investigation to enhance the understanding of duloxetine's broader implications for chemotherapy patients.

Evidence-Based Practice Question

Throughout this literature review, this team endeavored to answer the question: What is the effectiveness of duloxetine in the treatment plan of chemotherapy-induced peripheral neuropathy in cancer patients?

Review of Literature

An integrative literature review (IRL) is a nonexperimental design in which researchers critique, summarize, and conclude, in a way that is not influenced by personal bias, about the subject matter through a systematic search of peer-reviewed qualitative and quantitative research articles. Each article was appraised separately for its strengths and weaknesses before synthesizing and translating all data for applicability to the chosen subject matter.

Search Strategy

Search criteria were entered into the chosen databases. Search terms included chemotherapy-induced peripheral neuropathy AND duloxetine, CIPN AND duloxetine, chemotherapy-induced peripheral neuropathy AND CIPN AND neuropathic pain AND pharmacologic treatment, chemotherapy-induced peripheral neuropathy AND duloxetine AND quality of life, chemotherapy-induced peripheral neuropathy, AND duloxetine AND gynecologic cancer, CIPN AND psychological distress, AND sleep disturbances. Randomized control trials (RCTs), clinical trials, retrospective experimental, open-label pilot studies, pilot randomized trials, randomized cross-over trials, randomized placebo-controlled cross-over trials, cross- sectional studies, and clinical practice guidelines were included in this IRL. Search limiters included the publication year 2011-2023, peer-reviewed, human subjects, all adult age groups, English language, and full PDF text available. Inclusion criteria agreed on by this group were adult patients diagnosed with cancer suffering from chemo-induced peripheral neuropathy.

Exclusion criteria included studies not related to CIPN, studies lacking the use of duloxetine to manage symptoms, studies that did not isolate the benefits of duloxetine in their results, and studies describing predictors of efficacy of duloxetine rather than the actual results of use.

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) tool was used to organize search results for this IRL efficiently. Through The Nursing and Allied Health section of the online university library offered by Northwestern State University, the following databases were accessed: Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PubMed. Both databases were searched for relevant studies utilizing the filters and limitations previously stated.

Rationale for Search Strategy Limits

Search strategy limits are crucial in refining the scope of information retrieval, ensuring relevance and efficiency. By establishing parameters, we narrowed our search to specific domains, time frames, or content types, tailoring results most relevant to our research question. This enhances precision, saving time and effort. Moreover, limits help manage information overload, a common challenge in today's digital landscape. Setting constraints assists in focusing on pertinent data, reducing the likelihood of irrelevant or overwhelming results. Additionally, search strategy limits promote accuracy by excluding unrelated content, contributing to the reliability of the obtained information. These limits act as navigational tools, empowering our team to streamline our search process and extract valuable insights more precisely.

Search Results

After conducting an exhaustive search across selected databases, 15,996 articles were initially identified. Subsequently, after applying specific limiters, 15,871 articles were excluded, resulting in 145 articles for further consideration. During the initial phase of the article review, eight duplicate articles were removed, and an additional 93 articles were eliminated utilizing automation tools. This process yielded 52 articles for screening. Subsequently, requests for full texts were made via inter-library loan, resulting in 5 requests, of which three were not fulfilled, leaving 49 articles for further assessment. Further review identified three articles focusing on predictors of efficacy rather than the efficacy itself, while 14 articles failed to isolate the results specifically pertaining to duloxetine treatment. Moreover, 12 texts did not address duloxetine use with chemotherapy-induced peripheral neuropathy (CIPN), and four studies were excluded as they were not centered on human subjects.

Also, two articles were excluded due to the use of non-pharmacologic supplements instead of duloxetine. One study deviated from a psychological focus, and another was excluded due to an inappropriate study design. Ultimately, following the completion of this review process, 12 articles of high and good quality, which comprehensively discussed the effectiveness of duloxetine for treating CIPN, were deemed suitable for inclusion in this integrated review of literature (IRL).

CINAHL

The search terms chemotherapy-induced peripheral neuropathy and duloxetine were entered into the CINAHL database; this yielded 166 results. Once these results were acquired, limiters were applied for adult age groups, publication date, full-text availability, English language, and human subjects. Upon completion of this search, 23 articles were identified from CINAHL and imported to Rayyan for further screening for inclusion in this IRL.

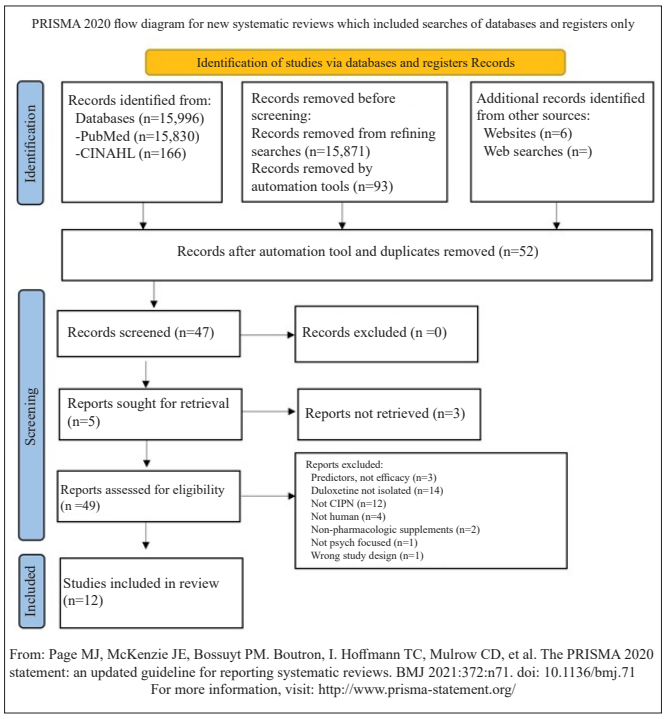
PubMed

The search terms were entered into the PubMed database and combined in the same manner as the search conducted in CINAHL. Once limiters were applied, including humans, the English language, and peer-reviewed articles, the combination of the following searches yielded articles reviewed for this IRL. Combined search terms CIPN and duloxetine yielded 25 results. The combination of chemotherapy-induced peripheral neuropathy and CIPN and neuropathic pain and pharmacologic treatment yielded 11 results. The combination of chemotherapy-induced peripheral neuropathy and duloxetine and quality of life yielded 29 results. The search terms chemotherapy-induced peripheral neuropathy, duloxetine, and gynecologic cancer yielded four results. Combined terms CIPN and depression

symptoms yielded 26 results. Lastly, combined search terms of CIPN and sleep disturbances yielded 27 results. The combination of searches produced 122 results from PubMed that were entered into Rayyan for further screening.

Supplemental Search Methods

Additional articles were used to formulate the background and significance of the IRL. Review articles and studies that did not populate automatically during database searches were searched manually. Relevant articles were retrieved from the following websites: American Cancer Society, American Society of Health-System Pharmacists, Upstate Medical University, and European Journal of Research and Medical Sciences. Utilizing this search method, four additional reports were added for review for potential use in this IRL.



Appraisal of the Literature

The accuracy of the review depends on the appraisal of the articles used on the IRL. Several appraisal tools were used in conducting this IRL to evaluate the quality of each article and exclude articles based on relevancy and quality. The appraisal tools used in this IRL included the Johns Hopkins (JH) Question Development tool, JH Individual Evidence Summary tool, (JH) Evidence Level and Quality Guide, Research Evidence Appraisal Tool, and JH Non-research Evidence Appraisal Tool.

Literature from the Discipline of Nursing

Smith et al. conducted a pivotal randomized, double-blind, placebo-controlled crossover trial aiming to evaluate the impact of duloxetine on average pain severity among patients with chemotherapy-induced peripheral neuropathy (CIPN) [3]. For this trial, duloxetine was administered at a daily dose of 60 mg. The research, carried out across eight National Cancer Institute (NCI)-funded cooperative research networks, included 231 participants aged 25 or above from April 2008 to March 2011, with follow-up completed in July 2012. Patients treated in community and academic settings were stratified based on the chemotherapeutic drug used and comorbid pain risk. In this clinical trial, patients were randomly assigned to two groups. One group received duloxetine followed by a placebo, while the other received a placebo followed by duloxetine. To be eligible, participants needed to have grade 1 or higher sensory neuropathy according to the NCI Common Terminology Criteria for Adverse Events and an average chemotherapy-induced pain score of at least four on a scale of 0 to 10, following paclitaxel, other taxanes, or oxaliplatin treatment. The initial treatment phase involved taking one capsule daily of 30 mg of duloxetine or a placebo for the first week, followed by two capsules of either 30 mg of duloxetine or a placebo daily for an additional four weeks.

The primary outcome measure was the mean decrease in average pain, assessed using the Brief Pain Inventory-Short Form "average pain" item. The results revealed a substantial reduction in pain severity among individuals receiving duloxetine as their initial 5-week treatment, with a mean decrease of 1.06 (95% CI, 0.72-1.40), compared to those who received a placebo (0.34; 95% CI, 0.01-0.66), resulting in a significant P-value of .003 and an effect size of 0.513. The observed mean difference in the average pain score between duloxetine and placebo was 0.73 (95% CI, 0.26-1.20). Notably, 59% of those initially receiving duloxetine reported decreased pain, compared to 38% in the placebo group.

In the context of nursing practice, this study bears relevance as it provides substantial evidence affirming the effectiveness of duloxetine in relieving pain associated with chemotherapy-induced peripheral neuropathy (CIPN). The statistical results highlight the significant impact of duloxetine, emphasizing its potential as a valuable intervention in the management of CIPN. Nurses can incorporate these findings into their clinical decision-making, considering duloxetine as a component of a comprehensive approach to enhance the overall well- being of patients undergoing chemotherapy. This study aligns with the nursing objective of optimizing symptom management and improving the quality of life for individuals grappling with the challenging side effects of cancer treatment.

Hirayama et al. conducted a pioneering open-label, randomized, crossover study to assess the efficacy of duloxetine in managing chemotherapy-induced peripheral neuropathy (CIPN) in Japanese patients [4]. The study's background information highlighted the difficulty in managing CIPN, with a notable absence of randomized trials on duloxetine for CIPN in Japan, despite a phase III trial in the United States demonstrating its effectiveness in treating CIPN following treatment with taxane and platinum-based chemotherapy agents. In this study, eligible patients underwent randomization into two groups. Group A was administered oral duloxetine, commencing with 20 mg/day for the initial week and increasing to 40 mg/day for the subsequent three weeks. In contrast, Group B received oral vitamin B12 (VB12) at 1.5 mg/day for four weeks. Following a 2- to 4-week washout period, the treatments were crossed over, with each group receiving the alternative treatment for an additional four weeks. The numbness and pain severity assessment was conducted using a visual analog scale (VAS).

The results from the study, involving 34 enrolled patients, demonstrated evident decreases in mean VAS scores for

numbness and pain during duloxetine administration. Statistical analysis revealed significant differences between the duloxetine-first (Group A) and VB12-first (Group B) groups concerning numbness ($p = 0.03$) and pain ($p = 0.04$) at four weeks after administration. Notably, fatigue was observed in 17.6% of participants.

The findings derived from this data indicate that duloxetine exerts a beneficial effect on chemotherapy-induced peripheral neuropathy (CIPN) induced by oxaliplatin, paclitaxel, vincristine, or bortezomib in Japanese patients. The statistical results underscore the significance of duloxetine in mitigating numbness and pain associated with CIPN. This study provides valuable insights into the potential efficacy of duloxetine within the Japanese population, urging further investigation into its role in managing chemotherapy-induced peripheral neuropathy. In the context of nursing practice, these findings lay the groundwork for considering duloxetine as a viable intervention for CIPN in Japanese patients, as it contributes to improving symptom management and the overall well-being of individuals undergoing chemotherapy in this specific demographic.

Jour Ebrahimiyan et al. conducted a study to evaluate the effectiveness of venlafaxine and duloxetine in managing chronic neurotoxicity induced by chemotherapy in cancer patients [5]. Chemotherapy-induced peripheral neuropathy (CIPN) poses a prevalent and challenging side effect in cancer treatment. The research involved cancer patients undergoing outpatient chemotherapy or hospitalization at Rasoul Akram hospital, employing a blind division of patients into two groups treated with venlafaxine and duloxetine, respectively. The treatment duration spanned ten weeks, with neuropathy severity assessed based on NCI Common Terminology Criteria for Adverse Events (CTCAE) v 3.0 criteria. The study, involving 30 patients (15 in each group), demonstrated a noteworthy decrease in neuropathy severity in the venlafaxine group compared to the duloxetine group during weeks 7 to 10. Notably, the results revealed that 75% and 85.7% of patients in the venlafaxine and duloxetine groups reported enhanced sleep patterns. The absence of significant differences in drug side effects between the two groups further reinforces the potential efficacy of venlafaxine.

In relation to nursing, this study contributes valuable insights into the management of chemotherapy-induced peripheral neuropathy, a critical concern in cancer care. The results imply that venlafaxine could be a suitable drug for treating chronic neurotoxicity with fewer side effects compared to other medications. However, the authors acknowledge the necessity for further prospective studies given the small sample size, emphasizing the ongoing importance of research to refine drug regimens and improve patient outcomes in oncology nursing practice. The study highlights the pivotal role of nurses in monitoring and managing chemotherapy-related side effects to optimize the overall well-being of cancer patients.

Salehifar et al. conducted a randomized, double-blind clinical trial to investigate the impact of pregabalin and duloxetine on the quality of life (QOL) of breast cancer patients experiencing taxane-induced peripheral neuropathy (TIPN) [6]. TIPN, a common side effect of adjuvant chemotherapy with taxanes, can significantly impact patients' QOL. The study, conducted in Sari, Iran, included breast cancer patients aged 18 or older who had received paclitaxel or docetaxel and experienced neuropathy grade one or higher, along with a neuropathic pain score of four or more. Participants were randomly assigned to receive either pregabalin or duloxetine for six weeks, with assessments of sensory neuropathy and QOL conducted at baseline and following treatment. Both interventions improved overall QOL compared to baseline, with no significant difference between the pregabalin and duloxetine groups after six weeks.

Notably, specific effects on QOL subscales were identified. Duloxetine showed a more favorable improvement in emotional functioning, while pregabalin was associated with greater enhancements in insomnia and pain scores. Statistically, the mean scores of the global health status/QOL scale for the pregabalin and duloxetine groups at baseline were 61 (SD: 5.11) and 60.28 (SD: 5.44), respectively ($P = 0.54$). After six weeks, both interventions were associated with a significant improvement in global QOL, and the scores did not differ significantly between the two groups.

In the context of nursing, this study offers valuable insight for healthcare providers involved in the care of breast cancer patients undergoing taxane-based chemotherapy. The findings highlight the effectiveness of both pregabalin and duloxetine in improving the overall QOL of patients experiencing TIPN. Nurses can collaborate with healthcare teams and consider the use of pharmacological options such as pregabalin and duloxetine to address specific aspects of taxane-induced peripheral neuropathy (TIPN) and improve the overall well-being of breast cancer patients. The findings of this study advocate for a patient-centered approach to symptom management, empowering nurses to make informed decisions in optimizing the quality of life (QOL) for individuals grappling with the challenging side effects of taxane-induced peripheral neuropathy.

Velasco et al. conducted an observational study to evaluate the efficacy and safety of duloxetine in 100 cancer survivors experiencing chemotherapy-induced peripheral neurotoxicity (CIPN) [7]. The severity of CIPN was assessed using grading systems such as TNSc and NCI-CTCv4, with the primary measure of duloxetine efficacy evaluated through the Patient Global Impression of Change (PGIC) scale. Importantly, the study considered a PGIC score greater than four, indicative of a clinically meaningful response.

The findings revealed that a significant proportion of patients experienced dropout from duloxetine, primarily due to either lack of efficacy (20%) or side effects (37%). Male patients were more likely to discontinue duloxetine due to lack of efficacy, highlighting potential gender- related variations in treatment response. PGIC scores were higher in female patients, those treated with taxanes, and those with short-lasting CIPN. The multivariate analysis identified female gender and short-lasting CIPN as independent factors associated with a favorable response to duloxetine.

In the context of nursing practice, this study offers crucial insights into the real-world experiences of cancer survivors undergoing duloxetine treatment for chemotherapy-induced peripheral neurotoxicity (CIPN). The challenges related to

tolerability, dropout rates, and factors influencing treatment response emphasize the complexity of managing CIPN. Nurses play a pivotal role in monitoring patients for treatment response, managing side effects, and providing support to those living with the lingering daily effects of CIPN. The study highlights the importance of tailoring interventions based on individual characteristics while remembering to consider factors such as gender and the duration of CIPN symptoms. As nursing professionals navigate the intricacies of symptom management in cancer survivors, the findings from this study contribute valuable information to enhance the quality of care provided to patients grappling with the aftermath of chemotherapy-induced peripheral neurotoxicity.

Yang et al. conducted an open-label pilot study aiming to assess the efficacy and tolerability of duloxetine, an antidepressant known for its effectiveness in treating diabetic neuropathic pain, in treating chronic oxaliplatin-induced peripheral neuropathy (OIPN) in patients with stage III or IV colorectal cancer [8]. This study was prompted by the lack of established treatments for chronic OIPN, leading to the exploration of duloxetine as a potential treatment. This study enrolled 39 patients with colorectal cancer and chronic OIPN. Duloxetine was administered, with the dose gradually increasing from 30 mg/day to 60 mg/day. Pain intensity was evaluated at baseline and 12 weeks after duloxetine post-treatment initiation, utilizing the visual analog scale (VAS) score and the National Cancer Institute Common Toxicity Criteria for Adverse Events, version 3 (NCI-CTCAE v3.0). The results indicated that 23.1% of patients discontinued duloxetine due to adverse events. However, among the remaining 30 patients, 63.3% experienced an improvement in VAS scores. Notably, 47.4% of these patients demonstrated a simultaneous grade improvement, while 52.6% maintained a stable grade according to NCI-CTCAE v3.0. The study concluded that duloxetine is a feasible treatment for chronic OIPN, demonstrating tolerable toxicity at a daily dose of 60 mg/day. Statistical findings highlighted the positive impact of duloxetine on pain reduction, as evidenced by the improvement in VAS scores. The study exhibits valuable insights into the potential role of duloxetine in managing chronic OIPN. These findings address a critical gap in available treatment options for this patient population.

For nursing practice, this evidence suggests that duloxetine could be considered as part of a comprehensive approach to alleviate chronic OIPN, thereby enhancing the quality of life for patients with colorectal cancer undergoing oxaliplatin-based chemotherapy. Further research and larger-scale studies may be warranted to solidify the understanding of duloxetine's effectiveness in this context.

Otake et al. conducted a retrospective study to assess the usefulness and adverse effects of duloxetine in treating paclitaxel-induced peripheral neuropathy (PIPN) in gynecological cancer patients [9]. The study aimed to evaluate the efficacy of duloxetine and identify potential factors associated with its effectiveness. The results, extracted from the medical records of 25 gynecological cancer patients undergoing duloxetine treatment, demonstrated that 56% of patients exhibited an improved response to duloxetine for paclitaxel-induced peripheral neuropathy (PIPN). Univariate and multivariate analyses were conducted to explore associations between various factors and the effectiveness of duloxetine treatment. Interestingly, factors such as patient age, tumor origin, chemotherapy regimen, accumulated doses of paclitaxel or carboplatin, previous medication, maintenance dosage, and timing of treatment with duloxetine were not found to be significantly associated with the drug's effectiveness. This demonstrates that duloxetine may effectively manage PIPN across diverse patient characteristics and treatment variables. Furthermore, the study underscores that the adverse effects of duloxetine were mild and well-tolerated, emphasizing the drug's safety profile in this patient population. These findings contribute valuable insights into the potential utility of duloxetine as a treatment option for PIPN in gynecological cancer patients.

For nursing practice, this study suggests that duloxetine could be considered as part of a comprehensive approach to alleviate PIPN, offering a potential option with minimal side effects. The results encourage further exploration and consideration of duloxetine in the management of chemotherapy-induced peripheral neuropathy, particularly in the context of gynecological cancer treatment.

Literature from the Discipline of Psychology

According to Hong et al., increased neurotoxicity scores were associated with depression, anxiety, and low sleep quality [10]. This study's purpose was to identify the level of effects chemotherapy-induced peripheral neuropathy had on psychological distress and sleep disturbances in 706 patients newly diagnosed with cancer. The methods utilized in the study include the Patient Neurotoxicity Questionnaire (PNQ), the Pittsburgh Sleep Quality Index (PSQI), the Distress Thermometer (DT), and the Hospital Anxiety and Depression Scale (HADS). For the study, 706 patients newly diagnosed with cancer were interviewed using a cross-sectional survey. The measurements of CIPN, sleep quality, and psychological distress were obtained from each patient after the 4th week of receiving chemotherapy. Approximately 90% of patients receiving chemotherapy experienced CIPN symptoms at a certain point during their cancer treatment. Results were concluded after correlation coefficients were calculated between various questionnaire results, which include ($p < 0.0001$) between the PNQ total and the DT (distress thermometer). Symptoms measured by the PNQ, grades D and E, which are moderate to severe intensity, were significantly associated with diminished sleep quality and poor psychological status.

The data collected from this study can be translated to advanced nursing practice by implementing pertinent mental health screening tools as a requirement for the initial assessment of a patient newly diagnosed with cancer. Collecting baseline data related to their mental health status before initiation of chemotherapy is an imperative part of treatment so that the provider can reassess the mental health scores in intervals and apply changes to treatment in response to negative mental health scores. An elevated PSQI and Distress Thermometer score can be directly affected by uncontrolled CIPN.

Souza et al. conducted a cross-sectional study to assess depressive symptoms related to chemotherapy regimens and bring attention to the importance of psychological distress' effect on cancer treatment compliance [11]. A quantitative approach

was utilized in this study to assess depressive symptoms in 112 women diagnosed with breast cancer and receiving chemotherapy. This study used multiple reliable psychological screening questionnaires to collect subjective data. The Morisky Test and Beck Depression Inventory were used with structured interviewing to collect subjective and objective data.

This study showed that approximately 46.43% of patients demonstrated a lack of adherence to their treatment [11]. The Morisky Test and Beck Depression Inventory were used with structured interviewing to collect subjective and objective data.

According to the data collected, there was a high association of diminished treatment adherence in the patients who were experiencing depression and psychological distress related to adverse symptoms secondary to their chemotherapy. These numbers were traced directly to patients who admitted to low-quality sleep, pain related to neuropathy, and decreased quality of life due to these unwanted side effects.

This mental health-focused study can be applied to treatment planning for chemotherapy patients to potentially create early screening protocols for psychological distress in cancer patients.

Mahfouz et al. conducted a cross-sectional study to assess the association between sleep dysfunction and CIPN severity [12]. The quality of life was also considered for patients who reported severe CIPN symptoms that affected their sleep quality. Reliable questionnaires were used to collect data and feedback from each patient. Multiple tools and questionnaires were implemented in the study to obtain the results. Pittsburgh Sleep Quality Index (PSQI), Chronic Acquired Polyneuropathy Patient-Reported Index, CAP-PRI, was used to obtain quality of life scores based on their mental and physical well-being, severity of CIPN, and social functioning.

The study enrolled 87 patients after the completion of their chemotherapy regimen. 77 of the 87 patients reported CIPN symptoms. 61 % of the patients' neuropathy severity was graded moderate to severe according to the NCI-CTCAE. Seventy-five percent of participants experienced sleep disturbance and poor-quality sleep associated with CIPN severity, resulting in decreased daily functioning.

This information can be applied to nursing practice by emphasizing the importance of CIPN pain control and assessment of the pain's interference with daily functioning and sleep, which supports an individual's mental well-being. Lack of sleep in an individual is detrimental to their health and potentially reduces successful outcomes when combined with an aggressive chemotherapy regimen.

Synthesis of the Literature

This IRL sought to answer the question: What is the effectiveness of duloxetine in the treatment plan of chemotherapy-induced peripheral neuropathy in cancer patients? The nursing and non-nursing database articles that were investigated revealed critical concepts associated with CIPN, including comorbid psychological effects such as depression, the detrimental and debilitating effects on QoL, and how APNs play a crucial role in the comprehensive management of this patient population.

Themes from the Nursing Discipline

Nursing literature focused on diagnosing and treating CIPN, QoL, pain control, and patient education. All articles are good to high quality with Level I, II, and III evidence. The themes identified across all nursing literature were diagnosis of CIPN, QoL, pain control, and patient education.

CIPN

The first recognized theme across nursing literature is the diagnosis of CIPN. CIPN is a result of damaged nerves caused by chemotherapy and other drugs used to treat cancer [1]. Patients suffering from CIPN may notice signs of nerve damage, such as burning, numbness, weakness, or pain in their hands and feet. It is thought that 50-90% of patients receiving chemotherapy are affected by CIPN, with 30-40% of those bearing a substantial risk of chronicity [2]. This theme provides an overview of the research and lends data to help support the importance of diagnosis and evidence-based treatment recommendations. This IRL prioritizes this issue because there is no known cure for CIPN. It creates challenges through treatment and treatment adherence because of the detrimental effects and impact on patients' well-being and QoL.

Quality of Life

The second major theme identified was QoL. Since CIPN is highly prevalent in cancer patients treated with chemotherapy, living with the daily symptoms of CIPN can be a significant source of distress for patients undergoing cancer treatment. According to Hershman et al., some individuals report burning or prickling sensations in the affected areas, motor symptoms such as weakness, or difficulty with fine motor skills such as buttoning shirts or picking up small objects [13]. There may also be loss of coordination, causing individuals to have trouble maintaining control and balance.

The QoL theme aligns with this IRL's goals of effective treatment of CIPN through duloxetine to reduce pain severity, treat peripheral sensory and motor symptoms, and improve overall function. With the potential to alleviate neuropathic symptoms, duloxetine helps manage life-altering symptoms of CIPN; therefore, improvement in quality of life is likely.

Pain Control

The third theme identified in this IRL is pain control. Duloxetine's role in managing pain and improving function makes it relevant to this theme. The primary outcome measure sought to decrease average pain using various pain assessment scores such as the Brief Pain Inventory Short Form and the Visual Analog Scale (VAS). This theme aligns with the IRL's goals by highlighting the significant impact of duloxetine and emphasizing its potential as a valuable intervention in the management of CIPN.

Patient Education

Patient education was the fourth theme relevant to this IRL and the nursing discipline.

Patient education and support is an essential component of APN practice. Incorporating duloxetine into a treatment plan requires educating patients on the benefits, potential side effects, and cost. Providing the risks and benefits of treatment empowers the patient to make informed decisions regarding their care. This encourages active participation in developing a treatment plan.

APNs are essential in the evaluation and diagnosis of patients suffering from CIPN. The practitioner should consider the disease process and the impact of its treatment on a patient, including their physical and mental health, daily living, and overall quality of life. Since there is no cure for CIPN, APNs often focus on symptom management. Living with the daily symptoms of CIPN can be a source of significant distress for patients undergoing cancer treatment [14]. Patient education is integral to how patients learn to live with CIPN.

Recommendations from the Discipline of Nursing

Considering the quantity, strength, and consistency of the nursing articles reviewed, there is evidence to support the efficacy of using duloxetine for the treatment of CIPN. Although evidence supporting the EBP was good to high quality, conflicting results suggest duloxetine as the only effective treatment for CIPN. APNs can confidently use these articles to treat patients with CIPN effectively. Each article consistently used QoL, pain control, and patient education themes. Of note, the American Society of Clinical Oncology recommends duloxetine as the standard of care in treatment for CIPN. The American Cancer Society recommends treatment for the relief of pain associated with CIPN, such as steroids, antidepressants, anti-seizure medications, opioids, and numbing patches/ creams. By assembling all characteristics of evidence, coupled with the research themes, the best evidence for effectively treating CIPN should focus on refining treatment protocols and considering individual patient characteristics.

The research on duloxetine use in patients with CIPN suggests several approaches for future exploration. To improve our understanding of its potential, future research should investigate comparisons with other pharmacological treatments commonly used for CIPN, such as venlafaxine or pregabalin.

Themes from the Discipline of Psychology

When reviewing literature from the discipline of psychology, themes that corresponded to the EBP question included CIPN, psychiatric symptoms of depression and anxiety, and sleep disturbance. Each article focused on CIPN and conditions that occur concomitantly due to its physical and mental effects on the patient receiving treatment. After the literature search, three articles focusing on psychological distress related to CIPN were included.

CIPN

The literature search focused on chemotherapy-induced peripheral neuropathy. CIPN is considered damage caused to the nerves outside of the brain and spinal cord [1]. CIPN is thought to affect 50-90% of cancer patients undergoing chemotherapy [2]. CIPN is responsible for declining QoL and the involvement of comorbid conditions such as depression. The theme across all data sources supports the need for prompt diagnosis and treatment of CIPN to prevent declining QoL and comorbid conditions.

Depression and Anxiety

The second theme identified, psychiatric symptoms of depression and anxiety, is associated with CIPN through the decline of QoL and increased pain intensity. CIPN has both physical and psychological ramifications. Psychological literature can provide insights into the psychological impact of CIPN, emphasizing the importance of addressing both physical and mental aspects in the treatment plan. Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI) commonly used to treat depression. This indicates that the mental health benefits are already well-researched and widely known for this medication. The efficacy of this duloxetine for treating both a physical and mental health diagnosis provides more benefit to an individual receiving chemotherapy with a considerable risk of CIPN development, particularly in the case where a pre-existing mental illness is present.

Unmanaged CIPN can result in multiple psychological stressors, including sensory impairment that contributes to sleep deprivation and increased fatigue [10]. It is also suggested that CIPN symptoms pose a continuous reminder to the patient that they do have cancer, therefore increasing their risk of depression and anxiety related to the treatment process [10]. Duloxetine should be strongly considered for CIPN patients experiencing severe pain and sensory impairment interfering with the patient's daily activities, including both necessary ADLs and leisure activities that provide enjoyment. According to Hong et al., patients are negatively affected by the inability to complete daily tasks on their own due to the severity of their chemo-induced neuropathy pain [10]. This potentially could result in decreased self-esteem and feelings of autonomy, which again increases the risk of psychological distress.

Sleep Disturbances

The third theme identified, sleep disturbance or insomnia, is a common condition associated with CIPN. The increased severity of CIPN is linked to a higher incidence of sleep disturbances in patients, which in turn results in increased fatigue, worsened neuropathy pain, and contributes to immunosuppression [10]. The neurotoxic effects of certain chemotherapy drugs may lead to disruptions in the central nervous system, affecting sleep-wake cycles [10]. This can result in difficulties falling asleep or staying asleep, impacting the overall sleep quality of individuals undergoing cancer treatment. A similar study revealed that patients who have received chemotherapy and experience moderate to severe CIPN have an increased prevalence of low-quality sleep due to neuropathy pain specifically [12]. Sleep disturbances can further contribute to psychological distress, creating a complex interplay between chemotherapy-induced neurotoxicity and the mental well-being of cancer patients.

Treatment Adherence

The fourth theme identified is treatment adherence to the chemotherapy regimen. As stated, CIPN causes several complications for the patient during chemotherapy. The result of these symptoms then causes psychological distress in the patient. According to de Souza et al., patients who experience depression during cancer therapy are more likely to become non-compliant with their cancer treatment plan [12]. This, in turn, increases the risk of further cancer progression, recurrence, and failed treatment.

Recommendations from the Discipline of Psychology

Literature from the discipline of Psychology provided insights into the psychological impact of CIPN, emphasizing the importance of addressing physical and mental characteristics in

the treatment plan. The efficacy of this duloxetine for treating both a physical and mental health diagnosis provides more benefit to an individual receiving chemotherapy with a high risk of CIPN development. It is evident within the research that patients who experience depression during cancer therapy were more likely to become non-compliant with their treatment plan. The best recommendation is to include prompt diagnosis and initiation of treatment of CIPN with duloxetine to alleviate pain and improve quality of life while treating both physical and mental health symptoms.

Summary

The key concepts discussed connect the importance and relevance of CIPN diagnosis and treatment. The nursing literature discusses how patient education and prompt management of CIPN affect QoL and pain control. Non-nursing literature discusses the importance of the treatment of physical and mental health during and after chemotherapy treatment. The research synthesized shows promise in the use of duloxetine to treat CIPN. There was evidence supporting the need for patient education regarding the diagnosis and treatment of CIPN. Patient education is an essential component of APN practice. Providing the risks and benefits of treatment empowers the patient to make informed decisions regarding their care. Since there is no cure for CIPN, it can be a significant source of distress. Patient education is integral to how patients learn to live with CIPN.

Along with patient education, research proves that the prompt management of CIPN helps improve patient QoL and decrease pain. When reviewing non- nursing literature, it is understood that CIPN affects both the physical and mental health of an individual, which has a direct impact on their response to treatment.

Recommendations for Future Research on Duloxetine Use in Cancer Patients

The research on duloxetine use in cancer patients suggests several avenues for future exploration. Future investigations should include comparisons with other pharmacological interventions commonly used for chemotherapy-induced peripheral neuropathy (CIPN), such as venlafaxine or pregabalin. This comparative analysis would provide insights into the relative efficacy, tolerability, and long-term effects of duloxetine in this context [15].

Diversifying the scope of inquiry is crucial, and researchers are encouraged to explore the efficacy of duloxetine across various cancer types and among diverse patient populations. While existing literature predominantly focuses on specific cancer types, broader studies encompassing different cancers and demographic groups would bolster the generalizability of findings.

The optimal timing and duration of duloxetine administration during chemotherapy represent another area warranting investigation. Understanding the most effective treatment windows could guide clinicians in maximizing the drug's preventive or therapeutic effects on CIPN, thereby optimizing patient outcomes.

Furthermore, a comprehensive investigation into the long-term effects and safety profile of duloxetine in cancer survivors is warranted. Assessing the impact of neurotoxicity beyond the acute treatment phase is imperative to ensure sustained patient well-being.

Considering combination therapies is a prudent avenue, with researchers advised to explore the potential benefits of integrating duloxetine with other pharmacological or non- pharmacological interventions for CIPN. Combinatorial approaches may yield synergistic effects, presenting a promising avenue for enhanced symptom management.

The inclusion of patient-reported outcomes is underscored, focusing on parameters such as quality of life, functionality, and treatment satisfaction. Incorporating patients' perspectives into research outcomes can guide future clinical practices, fostering a more patient-centered approach.

Lastly, conducting health economic analyses is recommended to evaluate the cost-effectiveness of integrating duloxetine into the management of CIPN. Understanding the financial implications will empower healthcare systems to make informed decisions about resource allocation to pursue comprehensive patient care.

In summary, future research on duloxetine in cancer patients should focus on refining treatment protocols, exploring its long-term effects, and considering individual patient characteristics. The impact on advanced nursing practice lies in embracing a holistic care approach, fostering interdisciplinary collaboration, and advocating for personalized, evidence-based care to optimize outcomes for cancer patients with chemotherapy-induced peripheral neuropathy.

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