Chemotherapy Induced Peripheral Neuropathy: Influence of Gabapentin On Quality Of Life

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ABSTRACT

Background: *Chemotherapy-induced peripheral neuropathy (CIPN) is a debilitating side effect of neurotoxic chemotherapy agents, significantly affecting patients' quality of life (QoL). Gabapentin, a gamma-aminobutyric acid (GABA) analogue, has been explored as a potential intervention to mitigate CIPN-related symptoms. However, its efficacy in improving QoL remains debated.*

Aim: *This study aims to evaluate the influence of gabapentin on the QoL of patients experiencing CIPN secondary to chemotherapy.*

Patients and Methods:*A prospective, randomized controlled trial was conducted at Zagazig university hospitals over a 1 year. A total of 74 patients diagnosed with CIPN following chemotherapy were recruited and randomized into two groups: a gabapentin-treated group and a control group receiving standard care. Patients were assessed using validated neuropathy and QoL scales at baseline and post-intervention. The primary endpoints included changes in neuropathic pain scores, functional impairment, and overall QoL, with data analyzed using appropriate statistical methods.*

Results: *Data indicate that gabapentin administration led to a significant reduction in neuropathic pain scores compared to the control group. Patients receiving gabapentin also reported improvements in functional outcomes, particularly in sensory and motor domains, as demonstrated by increased scores on QoL assessments. Furthermore, Results highlight a notable decrease in symptom severity, while findings reveal a correlation between pain reduction and overall QoL enhancement.*

Conclusion: *Gabapentin appears to effectively alleviate neuropathic pain and improve QoL in patients with CIPN. These findings support its role as a potential adjunct therapy for managing CIPN-related symptoms. Further large-scale studies are warranted to validate these results and refine treatment protocols*

Keywords*:* Chemotherapy, Induced Peripheral Neuropathy, Gabapentin,Quality Of Life

INTRODUCTION

Breast cancer remains the most prevalent malignancy among women and a leading cause of cancer-related mortality worldwide. Annually, over 1.5 million women, constituting approximately 25% of all female cancer cases, receive a breast cancer diagnosis [1]. Conversely, male breast cancer is a rare entity, with an estimated lifetime risk of 1 in 726, accounting for nearly 1% of all breast cancer cases [2].

In Egypt, breast cancer ranks as the second most common malignancy after liver cancer, collectively contributing, along with bladder cancer, to nearly 46% of all cancer cases. Among Egyptian women, breast cancer incidence is highest in Upper Egypt (38.7%), followed by Lower Egypt (33.2%) and Middle Egypt (26.8%) [3]. Although its incidence has risen over recent decades, mortality rates have declined due to advancements in screening, early detection, public awareness, and the evolution of therapeutic strategies [4].

Chemotherapy-induced peripheral neuropathy (CIPN) represents one of the most prevalent neurological complications of chemotherapy, affecting approximately one-third of patients receiving neurotoxic agents [5]. It manifests as both central and peripheral neurotoxicity, with clinical presentations ranging from mild neurocognitive impairment to severe encephalopathy [6]. CIPN significantly impacts functional capacity, reduces quality of life (QoL), and often necessitates dose reductions or discontinuation of chemotherapy. Furthermore, it remains a major dose-limiting toxicity among cancer survivors [7].

Currently, treatment options for CIPN remain limited, with available pharmacological interventions primarily targeting symptomatic relief rather than disease modification. Given the improved survival rates among cancer patients, early recognition and intervention are critical to mitigating severe neuropathy. However, no definitive causative therapy for CIPN prevention has been established [8].

Nerve conduction studies (NCS) serve as a reliable, objective, and non-invasive diagnostic tool for detecting neuropathic alterations. Longitudinal NCS assessments during chemotherapy have demonstrated persistent sensory nerve dysfunction, underscoring its role in CIPN pathogenesis. Additionally, peripheral nerve ultrasound is increasingly utilized for evaluating both mono- and polyneuropathies [9].

Gabapentin, an antiepileptic agent, exhibits high-affinity binding to voltage-gated calcium channels, modulating neurotransmitter release and serotonin levels. It has demonstrated efficacy in various neuropathic pain conditions, including diabetic neuropathy, postherpetic neuralgia, and spinal cord injury, making it a potential candidate for CIPN management [10].

This study aims to evaluate the impact of gabapentin on the quality of life (QoL) in patients with chemotherapy-induced peripheral neuropathy (CIPN). Specifically, it seeks to assess the effectiveness of gabapentin in alleviating neuropathic pain, improving functional capacity, and enhancing overall QoL in individuals undergoing chemotherapy.

Patients and Methods

Study Design and Setting

This randomized controlled clinical trial was conducted at the Clinical Oncology & Nuclear Medicine Department and nerve conduction studies were performed at the Rheumatology & Rehabilitation Department of Zagazig University Hospitals. Patients were randomly selected from those attending the department, provided they met the eligibility criteria and provided written informed consent after being informed about potential risks and complications. IRB#:101056-5-9-2023

Sample Size and Patient Groups

A total of 74 breast cancer patients were prospectively enrolled and randomized into two groups. Group A comprised 37 patients who received taxane-based chemotherapy in combination with gabapentin, whereas Group B included 37 patients who underwent taxane-based chemotherapy with a placebo.

Eligibility Criteria

Patients who were eligible for the study had a histologically confirmed diagnosis of invasive ductal carcinoma (IDC) of the breast, with no evidence of distant metastases at the time of diagnosis. They were between 18 and 70 years old and had adequate hematologic function, defined as hemoglobin levels of at least 10 g/dL, a platelet count of 100,000/μL or higher, and a white cell count (WCC) of at least 3,000/μL. Additionally, all participants had provided signed informed consent before enrollment, ensuring their understanding and willingness to participate in the study.

Patients were excluded from the study if they had a history of diabetes mellitus, used neurotoxic drugs beyond the study protocol, or had chronic liver or renal disease. Those with a synchronous second primary malignancy or confirmed distant metastases were also ineligible. Pregnancy was a contraindication, and individuals with psychiatric disorders that impaired their ability to provide informed consent were excluded. Additionally, patients older than 70 years were not included to maintain study safety and integrity.

Study Protocol

Patients prospectively received taxane-based chemotherapy as part of a clinical trial.

Pre-Treatment Assessment:

Before chemotherapy initiation, all patients underwent a comprehensive evaluation, including a full physical examination, hematological and biochemical laboratory tests, breast imaging (mammography

and ultrasound), chest imaging, and computed tomography (CT) of the abdomen and pelvis. Nerve conduction studies (NCS) were performed to assess motor and sensory function and exclude polyneuropathy as a factor affecting their quality of life. Quality of life (QoL) was assessed using subjective neuropathic pain questionnaires and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30).

Treatment Plan:

Group A received a 12-week regimen of taxane-based chemotherapy combined with gabapentin, while Group B received an identical chemotherapy regimen with a placebo. Gabapentin dosing was initiated at 300 mg on the first day of chemotherapy, increased to 600 mg on the second day, and further escalated to 900 mg on the third day, maintaining this dose throughout the chemotherapy course. (HRQoL) assessments before chemotherapy initiation and one month after treatment completion.

During-Treatment Evaluations:

Patients underwent routine hematological and biochemical evaluations before each chemotherapy cycle to monitor treatment tolerance and adverse effects.

Post-Treatment Assessment:

After completing chemotherapy, patients underwent a full physical examination, repeat laboratory evaluations, breast imaging (mammography and ultrasound), chest imaging, and abdominal and pelvic CT. Follow-up QoL was reassessed using neuropathic pain questionnaires and the EORTC QLQ-C30.

Statistical Analysis

Data analysis was performed using SPSS (Statistical Package for the Social Sciences), version 28. Categorical variables were expressed as absolute frequencies and analyzed using the chi-square test or Fisher's exact test when appropriate. The Shapiro-Wilk test was applied to assess data normality. Continuous variables were presented as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on distribution.

Between-group comparisons of continuous variables were conducted using the independent t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. Changes over time within the same group were analyzed using McNemar's test for binary categorical data and the paired t-test for continuous normally distributed data. A p-value <0.05 was considered statistically significant, while a p-value ≤ 0.001 was deemed highly significant.

Results

Table 1: Patient characteristics of the studied breast cancer patients (N=74).

Basic characteristics		All studied patients (N=74)
	NO.	%
Age group		
≤35 years	28	37.8%
>35 years	46	62%
Hypertension		
Absent	20	27%
Present	54	73%
Laterality		
Right	30	42%
Left	44	58%
ECOG		
1	50	67.5%
2	24	32.4%
Stage		
II	29	39.2%
III	45	60.8%
Tumor grade		
I	12	16.2%
II	37	50%
III	25	33.7%
Surgery		
MRM	44	59.4%
Conservative	30	40.5%
Protocol		
Neoadjuvant	20	27%
Adjuvant	54	73%
Molecular subtype		
Luminal	30	40%
HER2 +	20	27%
Basal like	24	32.4%

Among the 74 studied breast cancer patients, 37.8% were aged 35 years or younger, while the majority (62%) were older than 35. Hypertension was present in 73% of the patients, whereas 27% had no history of hypertension. All patients had not polyneuropathy by NCS. Regarding tumor laterality, 42% of cases were in the right breast, and 58% were in the left breast. In terms of performance status, 67.5% of patients had an ECOG score of 1, while 32.4% had a score of 2. The distribution of cancer stages showed that 39.2% were diagnosed at stage II, while 60.8% were at stage III. Tumor grading revealed that 16.2% of patients had grade I tumors, 50% had grade II, and 33.7% had grade III. Surgical intervention included modified radical mastectomy (MRM) in 59.4% of cases, while 40.5% underwent

conservative surgery. Regarding treatment protocols, 27% received neoadjuvant therapy, whereas 73% underwent adjuvant therapy. Molecular subtype analysis classified 40% of cases as luminal, 27% as HER2-positive, and 32.4% as basal-like.

Table 2 Quality-of-life assessment.

	Group A	**Group B**	**T**	**p**
	N=37 (%)	**N=37 (%)**		
Physical				
Pre	68.32 ± 08.23	68.78 ± 7.58	-0.25	0.804
Post	65.54 ± 8.09	59.16 ± 7.3	3.561	<0.001**
p¥	<0.001**	<0.001**		
Psychological				
Pre	67.14 ± 5.97	68.41 ± 9.87	-0.677	0.501
Post	63.81 ± 5.89	59.04 ± 9.87	2.516	0.015*
p¥	<0.001**	<0.001**		
Social functioning				
Pre	60.57 ± 12.25	63.14 ± 10.06	-0.985	0.328
Post	57.22 ± 8.99	51.38 ± 8.99	2.395	0.019*
p¥	<0.001**	<0.001**		
Environmental				
Pre	55.89 ± 10.91	59.43 ± 10.21	-1.442	0.155
Post	52.78 ± 10.55	49.11 ± 8.62	1.642	0.105
p¥	<0.001**	<0.001**		
All parameters				
Pre	62.98 ± 5.42	65.69 ± 4.7	-0.007	0.995
Post	59.84 ± 5.07	54.68 ± 4.54	4.617	<0.001**
p¥	<0.001**	<0.001**		

§ paired sample t test t independent sample t test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

The quality-of-life assessment compared Group A and Group B across physical, psychological, social functioning, and environmental domains both before and after the intervention. In the physical domain, the pre-intervention scores were similar between Group A (68.32 ± 8.23) and Group B (68.78 ± 7.58), but post-intervention, Group A showed a smaller decline (65.54 ± 8.09) compared to Group B (59.16 ± 7.3), with a statistically highly significant difference ($p < 0.001$). In the psychological domain, Group A had a pre-score of 67.14 ± 5.97 and a post-score of 63.81 ± 5.89, whereas Group B declined from

68.41 ± 9.87 to 59.04 ± 9.87, with a significant difference between groups (p = 0.015). Similarly, in the social functioning domain, Group A's score decreased from 60.57 ± 12.25 to 57.22 ± 8.99, while Group B had a greater reduction from 63.14 ± 10.06 to 51.38 ± 8.99, showing a statistically significant difference (p = 0.019).

The environmental domain showed a pre-score of 55.89 ± 10.91 and a post-score of 52.78 ± 10.55 in Group A, whereas Group B started at 59.43 ± 10.21 and dropped to 49.11 ± 8.62, though the difference was not statistically significant (p = 0.105). When analyzing overall quality-of-life parameters, Group A had an initial score of 62.98 ± 5.42, which declined to 59.84 ± 5.07 post-intervention, while Group B dropped more significantly from 65.69 ± 4.7 to 54.68 ± 4.54, with a highly significant difference (p < 0.001). Paired sample t-tests within each group revealed statistically significant reductions in all domains pre- and post-intervention (p < 0.001), highlighting an overall decline in quality of life, with Group B experiencing a more pronounced deterioration.

Table 3: Percent change in all parameters quality of life among studied groups:

% change	Group A	Group B	Z	p
	Median (IQR)	*Median (IQR)*		
Total	-4.5(-5.4, -3.96%)	-16.32(-18.7, -14.75%)	-7.368	<0.001**

Z Mann Whitney test IQR interquartile range **p≤0.001 is statistically highly significant

The percent change in overall quality-of-life parameters showed a significantly greater decline in Group B compared to Group A. The median percentage change in Group A was -4.5% (IQR: -5.4% to -3.96%), whereas Group B exhibited a much steeper decline with a median change of -16.32% (IQR: -18.7% to -14.75%). The Mann-Whitney test revealed a highly significant difference between the two groups (Z = -7.368, p < 0.001), indicating that the deterioration in quality of life was substantially more pronounced in Group B. These findings suggest that patients in Group B experienced a more severe negative impact on their overall well-being compared to those in Group A.

Discussion

Chemotherapy-induced peripheral neuropathy (CIPN) is a prevalent and debilitating complication of chemotherapy, particularly taxane-based regimens, significantly impairing patients' quality of life (QoL) [11]. The underlying pathophysiology involves chemotherapy-induced alterations in mitochondrial function, ion channels, and intracellular signaling pathways, culminating in neuroinflammation, DNA damage, and axonal degeneration. These effects predominantly impact peripheral sensory nerves but can also affect motor and autonomic neurons [12]. The severity of neurotoxicity varies among patients, with symptoms ranging from transient discomfort to chronic

neuropathic pain and irreversible nerve damage [13]. Taxanes, including paclitaxel and docetaxel, are among the most neurotoxic chemotherapeutic agents [14]. CIPN can necessitate dose reduction or discontinuation of chemotherapy, negatively influencing cancer treatment outcomes and long-term survivorship [15].

In this study, we investigated the role of gabapentin in mitigating the impact of CIPN on QoL in breast cancer patients receiving taxane-based chemotherapy. Our results demonstrated that gabapentin significantly reduced neuropathic pain severity and improved various QoL domains, including physical, psychological, and social functioning, as well as overall well-being. Patients in Group A (gabapentin-treated) experienced a significantly smaller decline in QoL compared to those in Group B (placebo-treated), reinforcing the potential role of gabapentin as a neuroprotective agent in CIPN management.

The findings of our study align with previous research. Patel et al. [16] reported that gabapentin effectively reduced higher-grade neuropathic pain, with patients experiencing a shift from severe to milder pain grades post-treatment.

The preventive role of gabapentin in CIPN was further supported by Salehifar et al. [20], who demonstrated that taxane-induced peripheral neuropathy (TIPN) was strongly associated with decreased QoL. Their study identified significant negative correlations between QoL parameters and neuropathy severity, highlighting the importance of early detection and management of CIPN. Song et al. [21] also observed improved QoL outcomes with gabapentin in a randomized placebo-controlled trial.

Our study supports the hypothesis that early intervention with gabapentin may mitigate CIPN severity and preserve QoL in patients undergoing taxane-based chemotherapy.

Conclusion

In conclusion, our study demonstrated that gabapentin effectively alleviates neuropathic pain and mitigates the decline in QoL among breast cancer patients receiving taxane-based chemotherapy. Compared to the placebo group, gabapentin-treated patients experienced significantly less deterioration across multiple QoL domains, supporting its potential role as an adjunctive therapy for CIPN management. While our findings align with several previous studies, conflicting evidence from other trials highlights the need for further large-scale, multicenter randomized controlled trials to establish definitive recommendations regarding gabapentin's efficacy in CIPN prevention and treatment. Future research should also explore optimal dosing strategies and combination therapies to enhance treatment outcomes for patients at risk of CIPN

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