Open Access

Original Article

Association of Paclitaxel Induced Neuropathy with Quality of Life of Patients with Non-Metastatic Breast Cancer

Masaba Masood, Muhammad Nadeem, Amna Masood*, Aamira Ali, Muhammad Umair Tufail**

Department of Medicine, Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Department of Paeds, Polyclinic Hospital Islamabad, Pakistan, **Department of Medicine, POF Hospital Wah Cantt, Rawalpindi Pakistan

ABSTRACT

Objective: To look for an association of Paclitaxel induced neuropathy with the quality of Life of patients with non-metastatic breast cancer.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Oncology Department, Combined Military Hospital, Rawalpindi Pakistan, from Nov 2021 to Feb 2022.

Methodology: The study included one hundred and twenty patients with diagnosed non-metastatic breast cancer taking Paclitaxel chemotherapy for more than one month. Peripheral neurotoxicity was assessed by a consultant oncologist based on the Eastern Cooperative Oncology Group (ECOG) score. In addition, quality of Life was recorded with the help of the World Health Organization Quality of Life (WHOQOL)-BREF scale in all the study participants and associated with the presence and severity of neuropathy.

Results: Out of 120 non-metastatic breast cancer patients using Paclitaxel for more than one month included in the study, 113 (94.2%) were female, while 7(5.8%) were male. 52(48.3%) had good quality of Life, while 68(51.7%) had poor quality of Life. 34(28.3%) had Grade-0 neuropathy, 54 (45%) had Grade-I, 30(25%) had Grade-II, and 2(1.6%) had Grade-III neuropathy. Statistical analysis showed that the presence and severity of neurotoxicity had a statistically significant relationship with poor quality of Life (p-value=0.001).

Conclusion: Many patients having breast cancer using Paclitaxel had the presence of neuropathy. The presence and severity of neuropathy are strongly associated with poor quality of Life in patients included in our study.

Keywords: Breast cancer, Neurotoxicity, Paclitaxel, Quality of life.

How to Cite This Article: *Masood M, Nadeem M, Masood A, Ali A, Tufail MU. Association of Paclitaxel Induced Neuropathy with Quality of Life of Patients with Non-Metastatic Breast Cancer. Pak Armed Forces Med J 2023; 73(3): 755-758. DOI: https://doi.org/10.51253/pafmj.v73i3.8349*

INTRODUCTION

Clinicians and pharmacists have been trying hard to look for novel options of treatment for cancers and constantly doing trials to weigh the risks and benefits of older and newer agents.[1] No treatment modality for cancer could be perfect or free from adverse effects.[2,3] Medications used for chemotherapy in various types of cancers have multi-system adverse effects and, though used for managing the primary illness, may have a marked negative impact on the overall quality of Life of patients.[4,5] Neurotoxic adverse effects leading to motor, sensory or mixed neuropathies have been studied extensively with several medications used in the management of cancer patients.[6,7]

Paclitaxel is a commonly used chemotherapeutic agent in patients with different types of cancer, including breast cancer.[8] One study concluded that weekly Paclitaxel is associated with neuropathic adverse effects, and dose reduction may help reduce this side effect.[9]

Correspondence: Dr Masaba Masood, Department of Medicine, Combined Military Hospital, Rawalpindi-Pakistan

Received: 08 Mar 2022; revision received: 25 Apr 2022; accepted: 28 Apr 2022

Pakistan bears a huge burden on patients with different stages of breast cancer. Therefore, locally this subject was evaluated from a different perspective, and an animal study was performed to look for various agents which could prevent this adverse effect at molecular levels.[10] Limited work has been done to look for the impact of Paclitaxel-induced neuropathy on the quality of Life of patients who have breast cancer. Therefore, the rationale of this study was to look for an association of Paclitaxel-induced neuropathy with the quality of Life of patients with non-metastatic breast cancer managed at the Oncology Department of Combined Military Hospital Rawalpindi.

METHODOLOGY

The comparative cross-sectional study was conducted at the Oncology Unit of Combined Military Hospital Rawalpindi from November 2021 to February 2022. Ethical Review Board approve the study (No: 206/3/22). The sample size was calculated using the WHO sample size calculator using the population proportion of neuropathy with Paclitaxel as 71.1%.[11] The non-probability consecutive sampling technique was used to gather the sample.

Inclusion Criteria: Patients aged 18 to 70 years, of either gender, who were taking Paclitaxel for non-metastatic breast cancer for more than one month were included in the study.

Exclusion Criteria: The study did not include patients with uncontrolled DM, HTN, or IHD taking any medications other than Paclitaxel, known to cause neuropathies. Patients using alternative medications or those diagnosed with neurological, neuro-surgical or immunological illness-causing neuropathies were also excluded. Patients giving a history of neuropathies with any aetiology before the start of Paclitaxel were also excluded.

Paclitaxel is an antimicrotubule agent used to manage various types of cancers. Previously it was given every three weeks but is currently administered in weekly dosage schedules. Twelve patients receiving this medication for over a month were included in the study. Peripheral neurotoxicity was assessed by a consultant oncologist based on the Eastern Cooperative Oncology Group (ECOG) score.[12] Patients were divided into four grades from zero to three based on clinical symptoms described in the ECOG score.[13]

World Health Organization Quality of Life (WHOQOL)-BREF scale is a 26 items scale that assesses an individual's perception of quality of Life in the following four domains: physical health, psychological, social relationships and environment. The mean scores of each domain were multiplied by 4 to make domain scores comparable with the scores used in the WHOQOL-100. Raw scores are converted into transformed scores through a specified table in the scoring manual. Transformed scores range from 4-20, with scores 4-12 denoting the poor quality of Life and scores 13-20 good quality of Life. On various occasions, WHOQOL-BREF has been used as a valid and reliable scale in the Pakistani population.[14]

Statistical Package for Social Sciences (SPSS) version 25.0 was used for the data analysis. Quantitative variables were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics. The *p*-value lower than or up to 0.05 was considered as significant.

RESULTS

Out of 120 non-metastatic breast cancer patients using Paclitaxel for more than three months and less than one year included in the study, 113(94.2%) were female, while 07(5.8%) were male. In addition, 52 (48.3%) had good quality of Life, while 68(51.7%) had poor quality of Life. Table-I summarizes the general characteristics of the study participants. 34(28.3%) had Grade-0 neuropathy, 54(45%) had Grade-I, 30(25%) had Grade-II, and 02(1.6%) had Grade-III neuropathy. Out of the total study participants, 33(27.5%) had stage-I, 48(40%) had stage-II and 39(32.5%) had stage-III breast cancer. Table-II shows the results of the statistical analysis. It was revealed that the presence and severity of neurotoxicity had a statistically significant relationship with poor quality of Life (*p*-value-0.001) among patients with non-metastatic breast cancer receiving Paclitaxel.

Table-I: Characteristics of Patients with non-metastatic Breast Cancer Receiving Paclitaxel (n=120)

Study Parameters	n(%)
Age (Years)	
Mean±SD	49.78±9.817
Range (min-max)	21-65
Gender	
Male	07(5.8%)
Female	113(94.2%)
Stage of Breast Cancer	
Stage I	33(27.5%)
Stage II	48(40%)
Stage III	39(32.5%)
Presence of Comorbid Illness	
No	59(49.2%)
Yes	61(50.8%)
Grade-s of Neuropathy	
Grade- 0	34(28.3%)
Grade- I	54(45%)
Grade- II	30(25%)
Grade- III	02(1.6%)
Quality of Life	
Good	52(48.3%)
Poor	68(51.7%)

Table-II: Relationship of various Factors Including Paclitaxel Induced Neuropathy with Poor Quality of Life (n=120)

	Good Quality of Life	Poor Quality of Life	*p*-value
Age			
<40 years	24(46.1%)	33(48.5%)	
>40 years	28(53.9%)	35(51.5%)	0.796
Stage of Illness			
I	15(28.8%)	18(26.4%)	
II & III	37(71.2%)	50(73.6%)	0.773
Presence of Comorbid Illness			
No	24(46.1%)	35(51.5%)	0.564
Yes	28(53.9%)	33(48.5%)	
Neuropathy			
Grade-0	24(46.1%)	10(14.7%)	
Grade-I	18(34.6%)	36(52.9%)	
Grade-II	10(19.2%)	20(29.4%)	0.001
Grade-III	0(0%)	02(2.9%)	

DISCUSSION

Most patients included in our study had some grade of neuropathy, adversely affecting the overall quality of Life of patients with breast cancer. Management of any cancer involves teamwork, and the goal of treatment in most cases is to control the illness and maintain a good quality of Life for patients. Paclitaxel-based regimens are routinely used in various malignancies, including breast cancer. They show a good response but at the cost of disturbing adverse effects. Therefore, we conducted this study intending to look for the association of Paclitaxel-induced neuropathy with the quality of Life of patients with non-metastatic breast cancer. Storey *et al.* reported that younger patients reported more neuropathic symptoms in the upper extremities than older patients, and they felt distressed even one year after treatment.[15]

Gadisa *et al*. came up with the findings that severe arthralgia/myalgia, peripheral neuropathy, and gastritis were reported more in patients who were administered Paclitaxel based regimen as compared to those who were administered with other regimens.[16] In addition, more than 70% of our patients had some grade of neuropathy which affected their quality of Life inversely.

Quality of life outcomes, including neuropathy-associated scale, was studied in breast cancer patients using Paclitaxel and Eribulin-based chemotherapeutic regimens conducted in 2019.[17] It. It was concluded that the Eribulin-based regime was better regarding neuropathic side effects and quality of Life than the Paclitaxel-based regime. In our study, we concluded that a significant number of non-metastatic breast cancer patients using Paclitaxel had the presence of neuropathy. Breast cancer patients of Ethiopia were studied for the impact of various chemotherapy side effects on the overall quality of Life of patients.[18] It was concluded that age, tumour stage and educational status of the patients, Grade≥2 fatigue, dysgeusia, constipation, oral mucositis, dry mouth, peripheral neuropathy, and skin hyperpigmentation affected the quality of Life in study participants. In our study, we only looked for the impact of neuropathy and other socio-demographic factors on quality of Life. We found out that only neuropathy was associated with poor quality of Life.

Poor quality of Life had been a consistent phenomenon in our study participants despite aggressive management at a tertiary care teaching set-up. There-fore, adverse effects like neuropathies due to chemotherapeutic agents should be considered early and addressed adequately to ensure a better quality of Life among cancer patients.

LIMITATIONS OF STUDY

First, we cannot generalize the study results, as it could not be ascertained that neuropathy was due to Paclitaxel and poor quality of Life was due to neuropathy. Multiple factors in these patients, including other medications and the disease, can cause neuropathies. Moreover, multiple factors could compromise the quality of Life and Paclitaxel-induced neuropathy.

CONCLUSION

The significant number of non-metastatic breast cancer patients using Paclitaxel had the presence of neuropathy. The presence and severity of neuropathy are strongly associated with poor quality of Life in patients included in our study.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MM & MN: Data acquisition, critical review, approval of the final version to be published.

AM & AA: Study design, drafting the manuscript, data interpretation, concept, approval of the final version to be published.

MUT: Critical review, data analysis, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin 2020; 70(1): 7-30. doi: 10.3322/caac.21590.
2. Abbas G, Shah S, Hanif M, Asghar A, Shafique M, Ashraf K, *et al*. Cancer prevalence, incidence and mortality rates in Pakistan in 2018. Bull Cancer 2020; 107(4): 517-518. doi: 10.1016/j.bulcan. 2019.12.011.
3. Pucci C, Martinelli C, Ciofani G. Innovative approaches for cancer treatment: current perspectives and new challenges. Ecancermedicalscience 2019; 13(1): 961-962. doi: 10.3332/ecanc 2019.961.
4. Altun İ, Sonkaya A. The Most Common Side Effects Experienced by Patients Were Receiving First Cycle of Chemotherapy.Iran J Public Health 2018; 47(8): 1218-1219.
5. Gordon-Williams R, Farquhar-Smith P. Recent advances in understanding chemotherapy-induced peripheral neuropathy. F1000Res 2020 ; 9: F1000. doi: 10.12688/f1000research.21625.1.
6. Tan AC, McCrary JM, Park SB, Trinh T, Goldstein D. Chemotherapy-induced peripheral neuropathy-patient-reported outcomes compared with NCI-CTCAE grade. Support Care Cancer 2019 ; 27(12): 4771-4777. doi: 10.1007/s00520-019-04781-6.
7. Timmins HC, Li T, Trinh T, Kiernan MC, Harrison M, Boyle F, *et al*. Weekly Paclitaxel-Induced Neurotoxicity in Breast Cancer: Outcomes and Dose Response. Oncologist 2021 ; 26(5): 366-374. doi: 10.1002/onco.13697.

8. Kırca K, Kutlutürkan S. Symptoms Experience and Quality of Life in the Patients With Breast Cancer Receiving The Taxane Class of Drugs. Eur J Breast Health 2018; 14(3): 148-155. doi: 10.5152/ejbh.2018.3785.
9. Kawashiri T, Inoue M, Mori K, Kobayashi D, Mine K, Ushio S, *et al*. Preclinical and Clinical Evidence of Therapeutic Agents for Paclitaxel-Induced Peripheral Neuropathy. Int J Mol Sci 2021; 22(16): 8733. doi: 10.3390/ijms22168733.
10. Ullah R, Ali G, Subhan F, Naveed M, Khan A, Khan J, *et al*. Attenuation of nociceptive and paclitaxel-induced neuropathic pain by targeting inflammatory, CGRP and substance P signaling using 3-Hydroxyflavone. Neurochem Int 2021 ; 144: 104981. doi: 10.1016/j.neuint.2021.104981.
11. Mizrahi D, Park SB, Li T, Timmins HC, Trinh T, Au K, *et al*. Hemoglobin, Body Mass Index, and Age as Risk Factors for Paclitaxel- and Oxaliplatin-Induced Peripheral Neuropathy. JAMA Netw Open. 2021 ; 4(2): e2036695. doi: 10.1001/jamanetworkopen.2020.36695.
12. Farrar MC, Jacobs TF. Paclitaxel. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023.
13. Azam F, Latif MF, Farooq A, Tirmazy SH, AlShahrani S, Bashir S, et al. Performance Status Assessment by Using ECOG (Eastern Cooperative Oncology Group) Score for Cancer Patients by Oncology Healthcare Professionals. Case Rep Oncol 2019; 12(3): 728-736. doi: 10.1159/000503095.
14. Malik M, Khan SA, Rana M, Khan F. Long term outcome of schizophrenia– A cross-sectional study. Pak Armed Forces Med J 2016; 66(4): 579-585.
15. Storey S, Cohee A, Von Ah D, Vachon E, Zanville NR, Monahan PO, *et al*. Presence and Distress of Chemotherapy-Induced Peripheral Neuropathy Symptoms in Upper Extremities of Younger and Older Breast Cancer Survivors. J Patient Cent Res Rev 2020 ; 7(4): 295-303. doi: 10.17294/2330-0698.1757.
16. Gadisa DA, Assefa M, Wang SH, Yimer G. Toxicity profile of Doxorubicin-Cyclophosphamide and Doxorubicin-Cyclophosphamide followed by Paclitaxel regimen and its associated factors among women with breast cancer in Ethiopia: A prospective cohort study. J Oncol Pharm Pract 2020 ; 26(8): 1912-1920. doi: 10.1177/1078155220907658.
17. Park YH, Im SA, Kim SB, Sohn JH, Lee KS, Chae YS, et al. Korean Cancer Study Group (KCSG). Phase II, multicentre, randomised trial of eribulin plus gemcitabine versus paclitaxel plus gemcitabine as first-line chemotherapy in patients with HER2-negative metastatic breast cancer. Eur J Cancer 2017 ; 86: 385-393. doi: 10.1016/j.ejca.2017.10.002.
18. Gadisa DA, Wang SH, Yimer G. The Impact of AC and AC-T Chemotherapy's Toxicities on Quality of Life Among Women with Breast Cancer in Ethiopia: A Prospective Patient-Reported Outcomes Study. Breast Cancer (Dove Med Press) 2021 ; 13: 107-132. doi: 10.2147/BCTT.S289014.