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Original Article

Comparison of Peripheral Neurotoxicity of Weekly Paclitaxel Versus Thrice Weekly Paclitaxel Chemotherapy Among Cancer Patients

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ABSTRACT

Objective: To compare peripheral neurotoxicity of weekly Paclitaxel vs thrice weekly Paclitaxel chemotherapy among cancer patients.

Study Design: Quasi-experimental study.

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

Methodology: We enrolled 200 patients with diagnosed malignancies taking Paclitaxel chemotherapy for more than three months and less than one year. They were divided into two groups: Group-A received Paclitaxel weekly while Group-B received this medication thrice weekly. Peripheral neurotoxicity was assessed by consultant oncologist on the basis of Eastern Cooperative Oncology Group score and patients in both groups were categorised into four grades from 0 to 3, on the basis of clinical symptoms described in ECOG score.

Results: Out of 200 cancer patients prescribed Paclitaxel, 67(33.5%) were male while 133(66.5%) were female, 107(53.5%) received Paclitaxel weekly while 93(46.5%) received thrice weekly, 65(32.5%) had Grade 0 neuropathy, 90(45%) had Grade-I, 42(21%) had Grade-II while 03(1.5%) had Grade-III neuropathy. Dosage schedule was not associated with presence and severity of neurotoxicity.

Conclusion: A significant number of cancer patients using Paclitaxel had presence of neuropathy in our study, regardless of weekly or thrice weekly dosing of Paclitaxel.

Key words: Cancer, Neurotoxicity, Oncology, Paclitaxel.

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INTRODUCTION

The rise in neoplastic conditions all over the world has become a challenge for clinicians, researchers and public health experts,[1] especially as epidemiological data from our part of world shows that the situation is equally dire in Pakistan.[2] Extensive research has been done recently regarding best treatment options for various malignant conditions and weighing the risks and benefits of older versus newer chemotherapeutic agents.[3] All therapeutic options used for treatment of neoplastic diseases have adverse effects, with chemotherapeutic agents being notorious for having multiple systemic side effects impacting overall health related quality of life of patients.[4] Neurotoxic adverse effects can be some of the most debilitating, often leading to motor, sensory or mixed neuropathies, even though they have been studied extensively with number of medications used in management of cancer patients.[5,6] Paclitaxel has a number of reported adverse effects with one study in 2021,[7] concluding that this medication with weekly dosage schedule was associated with neuropathic adverse effects occurring early during the course of treatment while other studies reported no significant difference in the rates of Grade 3 sensory neuropathy.[8,9] A local study from Pakistan investigated the anti-nociceptive and anti-inflammatory propensity of 3-Hydroxyflavone (3HF) in mice and the preventive effect of 3HF against Paclitaxel -induced peripheral neuropathy in rats.[10] While limited epidemiological or interventional data has been available regarding neurotoxic effects of Paclitaxel in Pakistan, our study aims to compare weekly Paclitaxel vs 3-weekly Paclitaxel chemotherapy to compare peripheral neurotoxicity among cancer patients.

METHODOLOGY

The quasi-experimental study was conducted at Oncology Unit of Combined Military Hospital (CMH), Rawalpindi, Pakistan, from February 2021 to November 2021 after taking ethical approval (via letter no 218/11/21) from Ethical Review Board of hospital.

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Sample size was calculated using the World Health Organization (WHO) sample size calculator, by using population prevalence proportion of neuropathy with Paclitaxel as 71.1%. Non-Probability purposive sampling technique was used.

Inclusion Criteria: Patients aged 18-70 years, from both genders, who were taking Paclitaxel alone in a weekly or thrice weekly schedules for any malignancy, for more than three months and less than one year, were included.

Exclusion Criteria: Patients with uncontrolled DM, HTN, IHD and taking any medications other than Paclitaxel known to cause neuropathies, using any alternative medications or those having diagnosed neurological, neuro-surgical or immunological illness causing neuropathies or giving history of neuropathies with any etiology before the start of Paclitaxel, were excluded.

As Paclitaxel is an antimicrotubular agent, given every three weeks but currently also administered in weekly dosage schedules,[12] we made two groups in the study according to the dosage schedule. Group-A received Paclitaxel weekly while Group-B received it thrice weekly (Figure). Peripheral neurotoxicity was assessed by consultant oncologist, did not know the group allocation of the patient, on the basis of Eastern Cooperative Oncology Group (ECOG) score, where patients were divided into four grades from 0-3 on the basis of set of clinical symptoms described.[13]

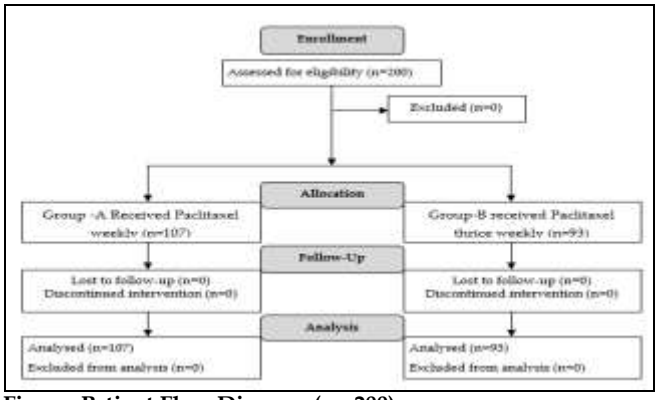

Figure: Patient Flow Diagram (n= 200)

Data was entered and analyzed by using Statistical package for Social Sciences (SPSS) version 23.0. The qualitative data were presented as frequency distribution and quantitative data were presented as Mean±SD. Relationship of various variables including dosage schedule with presence and severity of neurotoxicity was analyzed by using Pearson Chi-square test where p-value≤0.05 was considered statistically significant.

RESULTS

Out of 200 cancer patients included in the study, 67(33.5%) were male while 133(66.5%) were female. Mean age of the participants included in the study was 49.78±9.817 years, 107(53.5%) received weekly Paclitaxel while 93(46.5%) received thrice weekly Paclitaxel, 65(32.5%) had Grade 0 neuropathy, 90(45%) had Grade-I, 42(21%) had Grade-II while 03(1.5%) had Grade-III neuropathy. Out of patients who were administered Paclitaxel, 118(59%) had breast cancer, 34(17%) had ovarian cancer, 24(12%) lung cancer, 08(4%) had stomach cancer while 14(7%) had bladder cancer (Table-I).

Table-I: Characteristics of Patients Receiving Paclitaxel (n=200)

Study Parameters	n (%)
Age (years)	
Mean±SD	49.78±9.817 years
Range (min-max)	21 years-65 years
Gender	
Male	67(33.5%)
Female	133(66.5%)
Indications of Paclitaxel	
Breast cancer	118(59%)
Ovarian cancer	34(17%)
Lung cancer	24(12%)
Stomach cancer	08(4%)
Bladder cancer	14(7%)
Others	2(1%)
Dosage schedule	
Weekly	107(53.5%)
Thrice weekly	93(46.5%)
Grades of Neuropathy	
Grade 0	65(32.5%)
Grade I	90(45%)
Grade II	42(21%)
Grade III	3(1.5%)

Age, gender, duration of Paclitaxel use and dosage schedule were not statistically significant and not associated with presence or severity of neurotoxicity (Table-II).

DISCUSSION

Cancer patients undergo aggressive treatment strategies, but the underlying malignant disease and treatment options often leave the patients prone to various health problems with different classes of chemotherapeutic agents having diverse spectrum of adverse effects.[14] Paclitaxel, an antimicrotubular agent,

Table-II: Association of Various Factors with the Presence and Severity of Neurotoxicity Among the Study Patients (n=200)

Study Parameters	Grade 0	Grade I	Grade II	Grade III	*p*-value
Age					
< 40 Years	28(43.1%)	42(46.7%)	25(59.5%)	01(33.3%)	0.361
>40 Years	37(56.9%)	48(53.3%)	17(40.5%)	02(66.7%)	
Gender					
Male	21(32.3%)	28(31.1%)	17(40.5%)	01(33.3%)	0.761
Female	44(67.7%)	62(68.9%)	25(59.5%)	02(66.7%)	
Dosage Schedule					
Weekly	35(53.8%)	47(52.2%)	23(54.7%)	02(66.7%)	0.959
3- Weekly	30(46.2%)	43(47.8%)	19(45.3%)	01(33.3%)	
Paclitaxel Duration					
3-6 Months	47(72.3%)	63(70%)	33(78.5%)	01(33.3%)	0.383
6-12 Months	18(27.7%)	27(30%)	09(21.5%)	02(66.7%)	

is no exception to this and multiple side effects have been reported. Ghoreishi *et al*.[15] concluded that advancing age, body surface area and the status of positive progesterone receptors, were the risk factors for neurotoxicity related to Paclitaxel use in breast cancer, however, in our study, age and dosing schedule did not emerge as significantly related to development of neurotoxicity. A meta-analysis,[16] comparing weekly vs thrice weekly use, revealed that overall survival benefit was better in weekly regimen, with less reporting of almost all serious adverse effects including neuropathy in weekly regimen. However, both groups in our study had no statistical difference between them. Another meta-analysis,[17] found that that weekly therapy had less hematological and non-hematological adverse effects as compared to thrice weekly therapy. Our study results did not establish this difference as both dosage schedules had equal chances of having neurotoxicity. Another study,[18] also concluded that patients having weekly therapy were more at risk of having neuropathies and other adverse effects as compared to those having thrice weekly therapy.

CONCLUSION

Cancer patients using Paclitaxel had presence of neuropathy whereby presence and severity of neuropathy was not related to weekly or thrice weekly dosing of Paclitaxel.

Conflict of Interest; None.

Authors' Contribution

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

TML & ZAA: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZAA & MN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MH & AK: Conception, data acquisition, 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. https://doi.org/10.3322/caac.21590
2. Abbas G, Shah S, Hanif M, Asghar A, Shafique M, Ashraf K. Cancer prevalence, incidence and mortality rates in Pakistan in 2018. Bull Cancer 2020; 107(4): 517-518. https://doi.org/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: 961. https://doi.org/10.3332/ecancer.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 Faculty Rev-177. https://doi.org/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. https://doi.org/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. https://doi.org/10.1002/onco.13697
8. Huang TC, Campbell TC. Comparison of weekly versus every 3 weeks Paclitaxel in the treatment of advanced solid tumors: a meta-analysis. 2012. In: Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews York (UK): Centre for Reviews and Dissemination (UK). [Internet]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK114933/
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. https://doi.org/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. https://doi.org/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. https://doi.org/10.1001/jamanetworkopen.2020.36695
12. Farrar MC, Jacobs TF. Paclitaxel . [Updated 2021 Jul 19]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021.
13. Azam F, Latif MF, Farooq A. 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. https://doi.org/10.1159/000503095
14. Nurgali K, Jagoe RT, Abalo R. Editorial: Adverse effects of cancer chemotherapy: anything new to improve tolerance and reduce sequelae?. Front Pharmacol 2018; 9: 245. https://doi.org/10.3389/fphar.2018.00245
15. Ghoreishi Z, Keshavarz S, Asghari Jafarabadi M, Fathifar Z, Goodman KA, et al. Risk factors for Paclitaxel -induced peripheral neuropathy in patients with breast cancer. BMC Cancer 2018; 18(1): 958. https://doi.org/10.1186/s12885-018-4869-5
16. Mauri D, Kamposioras K, Tsali L, Bristianou M, Valachis A, Karathanasi I, et al. Overall survival benefit for weekly vs. three-weekly taxanes regimens in advanced breast cancer: a meta-analysis. Cancer Treat Rev. 2010; 36(1): 69-74. https://doi.org/10.1016/j.ctrv.2009.10.006
17. Gao G, Chu H, Zhao L, Gui T, Xu Q, Shi J, et al. A meta-analysis of Paclitaxel -based chemotherapies administered once every week compared with once every 3 weeks first-line treatment of advanced non-small-cell lung cancer. Lung Cancer 2012; 76(3): 380-386. https://doi.org/10.1016/j.lungcan.2011.12.001
18. Chan JK, Brady MF, Penson RT, Huang H, Birrer MJ, Walker JL, et al. Weekly vs. every-3-week Paclitaxel and carboplatin for ovarian cancer. N Engl J Med 2016; 374(8): 738-748. https://doi.org/10.1056/NEJMoa1505067