CHEMOTHERAPY INDUCED NAUSEA AND VOMITING (CINV): EFFICACY OF DIFFERENT ANTIEMETIC REGIMENS ACROSS EMETOGENIC RISK LEVELS

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ABSTRACT

OBJECTIVES

This audit aimed to determine the efficacy of different antiemetic regimens across emetogenic risk levels in managing chemotherapy-induced vomiting and nausea.

METHODOLOGY

This retrospective cross-sectional clinical audit was conducted at the Department of Oncology, Northwest General Hospital, Peshawar, from Jan to December 2024, involving 369 patients presenting for chemotherapy. Patients' demographic and clinical characteristics were collected from medical records or directly from patients regarding their last chemotherapy experience. Patients were receiving three antiemetic regimens: Triplet antiemetic regimen (Aprepitant + Ondansetron + Dexamethasone), Triplet regimen + Metoclopramide, and Triplet regimen + domperidone. The incidence of vomiting and nausea post-chemotherapy was assessed using a structured questionnaire. SPSS-25 was used for data analysis. The chi-square test was applied with a 5% significance level.

RESULTS

Out of 369 cancer patients receiving chemotherapy, the median age was 54 years (IQR=18), ranging from 14 to 87 years, with a majority being female 209(56.6%). Vomiting was reported in 57(15.4%) patients, primarily occurring within the first three days, 33(58%), peaking on day two. Most cases were mild (1-2 episodes/day) in 39(68%) patients, with severe vomiting (≥10 episodes/day) occurring in only 3(5.3%) patients. Nausea was reported by 111(30.1%) patients. Digestive system cancers 81(22%) and breast cancer 78(21.1%) were the most common cancer types. Vomiting was significantly associated with moderate-risk chemotherapy (p<0.0001), where the triplet + metoclopramide group had the highest incidence. (29/42 cases)(69%). Overall, patients in the triplet + domperidone group had a lower incidence of nausea (49/111)(44%) and vomiting (22/57)(38.6%) compared to the triplet + metoclopramide group, though differences were not always statistically significant (p=0.17 for vomiting, p = 0.008 for nausea). Vomiting was significantly associated with antiemetic regimen selection in digestive system cancers (p<0.0001) and blood cancers (p=0.032), whereas nausea was significantly associated with antiemetic regimen selection in digestive system cancers (p<0.0001).

CONCLUSION

The triplet + domperidone regimen was associated with lower observed rates of chemotherapy-induced nausea and vomiting. However, overall differences between regimens were not statistically significant (except in the moderate emetogenic risk group), suggesting that the treatments were generally comparable in effectiveness.

KEYWORDS: *Antiemetic Therapy, Nausea, Vomiting Triplet Regimen, Domperidone, Metoclopramide*

INTRODUCTION

Several genetic and molecular changes lead to the unchecked development and proliferation of cells in cancer, a disease that is diverse and complex. As a result, the tissue mass in the affected areas of the body rapidly increases.[1] Surgery, radiation, and chemotherapy remain the mainstays of therapy, despite the development of several treatment techniques.[2] The cornerstone of anti-cancer treatment is still chemotherapy. For the majority of advanced carcinomas, it is the first-line therapy approach.[3] Chemotherapy-induced nausea and vomiting (CINV) is one of the significant side effects that can be fatal for cancer patients during and after treatment, even though it is an essential traditional treatment for cancer patients. Depending on the degree of CINV, different prevention and treatment tactics are used.[4] According to the literature, the risk of CINV is 40%.[5], while some studies report the risk even higher, i.e., 70-80%.[6] Chemotherapeutic agents are ranked in international antiemetic guidelines based on the probability of inducing acute emesis in the absence of antiemetic prophylaxis: highly emetogenic chemotherapy (HEC), moderately emetogenic chemotherapy (MEC), low emetogenic chemotherapy (LEC), and minimally emetogenic chemotherapy.[7] The treatment goal for CINV should be to prevent the first episode. Once patients experience CINV, they are four times more likely to experience nausea and vomiting in subsequent cycles of chemotherapy. Clinically effective medications, such as 5-hydroxytryptamine type 3 receptor antagonists (5-HT3 RA), neurokinin one receptor antagonists (NK1 RA), dexamethasone, and antipsychotics, are currently available to prevent or treat CINV. Additionally, benzodiazepines and other medication groups, including cannabinoids, can be utilized to treat CINV.[8] different researchers have investigated the compliance of these recommended antiemetic drugs in their setup. For instance, a study by Aapro et al. in 2021 examined how closely antiemetic prescribing practices aligned with MASCC/ESMO guidelines across five European countries. Analyzing data from over 45,000 patients, the study found that recommended antiemetic combinations, specifically NK1RA, 5-HT3RA, and dexamethasone, were significantly underused. Only 18% of patients on cisplatin, 24% on anthracycline-cyclophosphamide (AC), and 7% on carboplatin received the complete guideline-recommended regimen. Surprisingly, 12% of patients received no antiemetic treatment.[9] A meta-analysis conducted by Zhang et al. in 2023 included 23 randomized controlled trials, comprising nearly 8,000 cancer patients, that evaluated the effectiveness of the triple combination of aprepitant, dexamethasone, and a 5-HT3 receptor antagonist on preventing CINV. The study found that this combination significantly increased the rate of complete relief from CINV across the acute, delayed, and overall phases compared with other treatments. It was particularly effective in reducing nausea in the delayed and overall phases.[10] Poorly managed CINV can lead to dehydration, malnutrition, and unplanned hospital readmissions, increasing the healthcare burden. Evidence-based antiemetic guidelines exist based on chemotherapy's emetogenic potential.[11] However, real-world practice often deviates from guidelines. Resource limitations and inconsistent adherence to guidelines may negatively impact patient outcomes. This clinical audit was conducted at the Oncology Department of Northwest General Hospital and Research Centre, Peshawar, to assess the efficacy of antiemetic regimens across various emetogenic risk levels and cancer types. The findings of the study help to identify gaps in practice and promote personalized, evidence-based supportive care for chemotherapy patients.

METHODOLOGY

This retrospective cross-sectional clinical audit was conducted at the Department of Oncology at Northwest General Hospital from January 2024 to December 2024. A total of 369 patients undergoing chemotherapy at our centre were included in the study. The sample size was calculated using OpenEpi software, with an anticipated CINV frequency of 40%, a 95% confidence level, and a 5% margin of error. Subgroup analyses based on emetogenic risk and cancer type were performed for exploratory purposes and were not powered for definitive subgroup comparisons. Data were gathered from two primary sources: direct patient reports on post-chemotherapy condition and the hospital's electronic medical record system, which provided clinical information and chemotherapy treatment data. Data regarding patient demographics, including age and gender; clinical variables such as cancer type and chemotherapy regimen administered; CINV, including whether patients experienced nausea or vomiting, the time of onset relative to chemotherapy, and symptom severity. Additionally, details regarding the antiemetic medications used were recorded. All the information was recorded in an SPSS file for data analysis. Data analysis was performed through SPSS-25. Mean ± SD or Median (IQR) was calculated for the quantitative variable after checking data normality using the Shapiro-Wilk test. Frequency and percentages were calculated for the categorical variable. The Chi-square test or Fisher's exact test was used to assess the association between CINV and different antiemetic regimens, as appropriate, across different chemotherapy risk groups.

RESULTS

In this study, 369 cancer patients receiving chemotherapy were included. The median age of the patients was 54.8 (IQR=18) years, ranging from 14 to 87 years, and the cohort was predominantly female (209, 56.6%). Among these patients, 57(15.4%) reported chemo-induced vomiting, with the most common onset, 33(58%), occurring within the first (1-3) days, among which the highest occurrence, 17(29%), was on the second day. A smaller number of patients reported vomiting after a week, with occurrences on the eighth day=7(12%), the tenth day=5(9%), the fourteenth day=2(3.5%), and the twenty-first day=3(5.2%), each affecting less than 2% of the patients receiving chemotherapy. Severity of vomiting varied, with most reporting mild (1-2 episodes/day, 39(68%)) to moderate (2-3 episodes/day, 15(26%)). Fewer patients reported more severe vomiting, with 10 episodes per day, 3(5.3%). Nausea was reported by 111(30.1%) after starting chemotherapy. The most common cancer types observed in this study were digestive system cancers (81, 22.0%) and breast cancer (78, 21.1%), followed by blood and lymphatic system cancers (67, 18.2%) and genitourinary cancers (61, 16.5%). The less common types were brain and nervous system cancers, lung cancer, and head and neck cancers. Table 1 Vomiting was reported by 15.4% of patients and was more frequently observed among those receiving the triplet + metoclopramide regimen (61.4%). A statistically significant association was identified in the moderate emetogenic risk group (p<0.0001), where vomiting was more commonly reported in patients receiving Metoclopramide (69%) compared with domperidone (31%). No statistically significant associations were observed in the minimal, low, or high emetogenic risk groups (Table 2). Similarly, nausea was reported by 30.1% of patients and was more frequent in the triplet + metoclopramide group (56%) than in the triplet + domperidone group (44%), with no cases among patients receiving the triplet regimen alone. A significant association was observed overall (p = 0.008), particularly within the moderate emetogenic risk category (p<0.0001), where nausea was more commonly reported with Metoclopramide (60%) than domperidone (40%). No significant associations were found in the minimal, low, or high-risk groups (Table 3). Across cancer types, variation in vomiting occurrence was observed among antiemetic regimens. In blood and lymphatic system cancers, a higher proportion of patients receiving Metoclopramide did not report vomiting (67.2%), whereas in digestive system cancers, vomiting was more frequently reported among patients receiving Metoclopramide (93.5%) (p<0.0001). When all cancer types were considered collectively, vomiting was less frequently reported in patients receiving domperidone compared with Metoclopramide, with a statistically significant association (p=0.017) (Table 4). With respect to nausea across cancer types, digestive system cancers showed a significant association between antiemetic regimen and nausea occurrence (p<0.0001), with nausea more commonly reported among patients receiving Metoclopramide (89.4%). In breast cancer patients, no statistically significant association was observed between antiemetic regimen and nausea (p = 0.96), with similar proportions of patients reporting no nausea across regimens. Overall, when all cancer types were analyzed together, nausea was less frequently reported in the domperidone group compared with the metoclopramide group, with a statistically significant association (p = 0.008) (Table 5).

Table 1: Patients Presented with Cancer Type

Cancer Type	N(%)
Blood & Lymphatic System Cancers	67(18.2%)
Bone Cancer	12(3.3%)
Brain & Nervous System Cancers	23(6.2%)
Breast Cancer	78(21.1%)
Digestive System Cancers	81(22.0%)
Genitourinary (Urinary & Reproductive) Cancers	61(16.5%)
Head & Neck Cancers	14(3.8%)
Lung Cancer	21(5.7%)
Non-Blood & Lymphatic System Cancers	03(0.8%)
Unspecified Site Cancer	09(2.4%)
Total	369(100.0%)

Table 2: Comparison of Vomiting Status among Different Antiemetic Regimens across Emetogenic Risk Levels

Emetogenic Chemotherapy	Vomit Status	Triplet antiemetic regimen	Triplet antiemetic regimen + Donperidone	Triplet antiemetic regimen + Metoclopramide	Total	P-Value
Minimal Risk	No	-	04(10.8%)	33(89.2%)	37	0.548[1]
	Yes	-	00(00%)	03(100%)	03	
Low Risk	No	-	52(61.2%)	33(38.8%)	85	0.747[1]
	Yes	-	06(66.7%)	03(33.3%)	09	
Moderate Risk	No	-	99(69.7%)	43(30.3%)	142	<0.0001[2]
	Yes	-	13(31%)	29(69%)	42	
High Risk	No	06(12.5%)	21(43.8%)	21(43.8%)	48	0.166[1]
	Yes	00(00%)	03(100%)	00(00%)	03	
Total	No	06(02%)	176(56%)	130(42%)	312	0.17[2]
	Yes	00(00%)	22(38.6%)	35(61.4%)	57	

[1]P-value was calculated through Fisher's Exact test. [2]P-value was calculated through the Chi-square test

Table 3: Comparison of Nausea Status among Different Antiemetic Regimens Across Emetogenic Risk Levels

Emetogenic Chemotherapy	Nausea Status	Triplet antiemetic regimen	Triplet antiemetic regimen+Donperidone	Triplet antiemetic regimen + Metoclopramide	Total	P-Value
Minimal Risk	No	-	03(8.3%)	33(91.7%)	36	0.292[1]
	Yes	-	01(25%)	03(75%)	04	
Low Risk	No	-	42(62%)	26(38%)	68	0.984[2]
	Yes	-	16(62%)	10(38.5%)	26	
Moderate Risk	No	-	85(73%)	32(27%)	117	<0.0001[1]
	Yes	-	27(40%)	40(60%)	67	
High Risk	No	06(16.2%)	19(51.4%)	12(32.4%)	37	0.071[1]
	Yes	00(00%)	05(35.7%)	09(64.3%)	14	
Total	No	06(2.3%)	149(57.8%)	103(39.9%)	258	0.008[2]
	Yes	00(00%)	49(44%)	62(56%)	111	

[1]P-value was calculated through Fisher's Exact test. [2]P-value was calculated through the Chi-square test

Table 4: Comparison of Vomiting Status among Different Antiemetic Regimens Across Cancer Types

Cancer type	Vomit Status	Triplet antiemetic regimen	Triplet antiemetic regimen + Donperidone	Triplet antiemetic regimen + Metoclopramide	Total	P-Value
Blood & Lymphatic System Cancers	No	03(4.7%)	18(28.1%)	43(67.2%)	64	0.032[1]
	Yes	00(00%)	03(100%)	00(00%)	03	
Brain & Nervous System	No	-	10(50%)	10(50%)	20	0.103[1]
	Yes	-	00(00%)	03(100%)	03	
Digestive System Cancers	No	-	24(48%)	26(52%)	50	<0.0001[1]
	Yes	-	02(6.5%)	29(93.5%)	31	
Genitourinary (Urinary	No	03(06%)	26(52%)	21(42%)	50	0.396[1]
	Yes	00(00%)	08(72.7%)	03(27.3%)	11	
Total	No	06(02%)	176(56.4%)	130(41.7%)	312	0.017[1]
	Yes	00(00%)	22(38.6%)	35(61.4%)	57	

[1]P-value was calculated through Fisher's Exact test.

Table 5: Comparison of Nausea Status among Different Antiemetic Regimens Across Cancer Types

Cancer types	Nausea Status	Triplet antiemetic regimen	Triplet antiemetic regimen + Donperidone	Triplet antiemetic regimen + Metoclopramide	Total	P-Value
Blood & Lymphatic System Cancers	No	03(4.9%)	18(29.5%)	40(65.6%)	61	0.54[1]
	Yes	00(0%)	3(50%)	03(50%)	06	
Brain & Nervous System	No	-	7(41.2%)	10(58.8%)	17	0.708[1]
	Yes	-	3(50%)	03(50%)	06	
Breast Cancer	No	-	47(77%)	14(23%)	61	0.96[1]
	Yes	-	13(76.5%)	04(23.5%)	17	
Digestive System Cancers	No	-	21(61.8%)	13(38.2%)	34	<0.0001[1]
	Yes	-	5(10.6%)	42(89.4%)	47	
Genitourinary (Urinary	No	03(7%)	23(53.5%)	17(39.55)	43	0.499[1]
	Yes	00(0%)	11(61.1%)	07(38.9%)	18	
Head & Neck Cancers	No	-	3(33.3%)	06(66.7%)	09	0.803[1]
	Yes	-	2(40%)	03(60%)	05	
Total	No	06(2.3%)	149(57.8%)	103(39.9%)	258	0.008[2]
	Yes	00(0%)	49(44.1%)	62(55.9%)	111	

[1]P-value was calculated through Fisher's Exact test. [2]P-value was calculated through the Chi-square test

DISCUSSION

Chemotherapy-induced nausea and vomiting (CINV) remains a common and challenging complication in oncology, affecting patients' quality of life and potentially influencing treatment adherence. In our study, the overall prevalence of nausea and vomiting was 30.1% and 15.4%, respectively, with most symptoms occurring during the acute phase, particularly within the first three days of chemotherapy. These observations are broadly consistent with previous reports, including Benlahrech et al. (2024), who reported a CINV prevalence of 79% during the delayed phase, and Fernández-Ortega et al. (2012), who observed nausea and vomiting in 31% and 45.1% of chemotherapy cycles despite prophylaxis.[12,13] Our data indicate that standard triple antiemetic regimens (5-HT3 RA, NK1 RA, and dexamethasone) are generally associated with reduced rates of CINV, though outcomes appear to vary when these regimens are combined with agents such as Metoclopramide or domperidone. In moderate emetogenic chemotherapy (MEC), nausea and vomiting were more frequently reported with Metoclopramide compared with domperidone, which differs from some earlier reports suggesting noninferiority of Metoclopramide in specific contexts.[14,15] In our cohort, domperidone was associated with lower observed rates of CINV in several cancer types, including digestive system malignancies, whereas Metoclopramide was associated with higher observed rates in the same group ($p<0.0001$). The role of triple antiemetic therapy in managing acute and delayed CINV has been reported in multiple studies. Simhadri et al. (2024) and Miura et al. (2013) observed complete response (CR) rates exceeding 95% in both phases using netupitant, palonosetron, and dexamethasone.[16,17] Similarly, Kaushal et al. (2015) and the meta-analysis by Zhang et al. (2023) suggest that triple regimens may offer advantages over double regimens in terms of symptom control.[18,10] In our study, patients receiving the standard triplet regimen alone reported relatively low rates of nausea and vomiting, though these findings are observational and unadjusted for potential confounders. Adherence to guideline-recommended antiemetic prophylaxis appears to remain suboptimal. Pluzanski et al. (2016) reported that only about half of patients globally receive guideline-consistent prophylaxis, and our observations may reflect similar trends, where regimen selection was not always aligned with emetogenic risk.[19] The Asia Pacific CINV study by Hsieh et al. (2015)20 found that 69% of patients achieved a complete response in the first chemotherapy cycle, indicating that there remains a substantial unmet need in CINV management. Our study adds observational data on the use of domperidone in combination with triple antiemetic therapy. While direct comparative trials are limited, domperidone's dopamine D2 antagonism suggests potential utility in targeting pathways not fully addressed by 5-HT3 and NK1 receptor antagonists. In this cohort, domperidone was associated with lower observed rates of nausea and vomiting compared with Metoclopramide in some cancer types. These findings highlight the need for further research to better define domperidone's role in contemporary antiemetic protocols, while also considering its cardiac safety profile. Although not evaluated in this study, recent literature also supports adding agents such as olanzapine, palonosetron, or rolapitant to triple regimens to improve delayed-phase CINV control.[21,22] These observations support broader recommendations for individualized antiemetic strategies that account for patient-specific factors, including age, gender, cancer type, and chemotherapy emetogenic potential.

LIMITATIONS

Our study has a retrospective design and partial reliance on patient recall, which may have introduced recall bias in reporting chemotherapy-induced nausea and vomiting; a lack of data on prior chemotherapy experiences; and unmeasured variables such as adherence to prescribed antiemetics and use of rescue medications. Moreover, while domperidone showed superior outcomes in our setting, concerns regarding its cardiac safety profile warrant caution and further evaluation. Additionally, subgroup analyses by emetogenic risk and cancer type were exploratory and not powered to detect statistically robust differences, which may limit the generalizability of these findings.

CONCLUSIONS

Our study supports the use of triple antiemetic therapy in routine clinical practice but highlights variability in outcomes associated with the additional use of Metoclopramide, particularly in moderate emetogenic regimens and gastrointestinal malignancies. In this cohort, domperidone was associated with lower observed rates of nausea and vomiting. These findings emphasize the need for individualized antiemetic selection based on emetogenic risk, cancer type, and drug tolerability, and support continued adherence to international guidelines and further evaluation of less commonly used antiemetic agents such as domperidone.

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AUTHORS CONTRIBUTION

Muhammad Umer Khayyam Azam - *Concept & Design; Data Acquisition; Drafting Manuscript; Supervision; Final Approval*
Bushra Haider - *Concept & Design; Data Acquisition; Data Analysis/Interpretation Drafting Manuscript; Final Approval*
Nadia Qazi - *Concept & Design; Data Acquisition; Drafting Manuscript; Critical Revision; Final Approval*

The authors accept responsibility for all aspects of the work and will ensure that any concerns regarding the accuracy or integrity of any part are properly investigated and resolved.