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Original Article

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Comparative Study of Efficacy and Safety of Olanzapine as Add-on Therapy to Conventional Regimen in Preventing Chemotherapy-induced Nausea and Vomiting

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ABSTRACT

Background: Chemotherapy-induced nausea and vomiting (CINV) are significant adverse effects that can severely diminish a cancer patient's quality of life and hinder their ability to adhere to and tolerate treatment. This study aims to assess the efficacy and safety of adding olanzapine, compared to placebo, to a standard antiemetic regimen of granisetron and dexamethasone for the prevention of CINV in cancer patients undergoing highly emetogenic chemotherapy.

Methods: The present study is a randomized, double-blind study of 82 cancer patients receiving highly emetogenic chemotherapy (HEC) which was conducted at a tertiary care hospital in India from June 2019 to February 2020, patients were randomized (1:1) into two groups and monitored for four days post-chemotherapy.

Results: The olanzapine group exhibited statistically significantly higher complete response rates than the placebo group at all measured time points. This superiority was observed during the early (0-24 hours), late (25-120 hours), and overall (0-120 hours) assessment periods. Both treatment approaches were well-tolerated, with only mild side effects reported.

Conclusion: Olanzapine, as compared with placebo, significantly improved nausea prevention, as well as the complete-response rate in CINV, among previously untreated patients who were receiving highly emetogenic chemotherapy (HEC).

Key-words: Cancer, Chemotherapy-induced Nausea and vomiting, Malignant neoplasm, Olanzapine

INTRODUCTION

Cancer is a leading cause of illness and death worldwide, affecting both developed and developing nations. [1] In 2018, it was the second leading cause of death globally, responsible for approximately 9.6 million deaths. [2-4]

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Data from 2012 shows that the most common cancers in men were lung (12.0%), mouth (11.4%), prostate (7.0%), and tongue (7.06%) cancers. For women, the most prevalent cancers were breast (21.0%), cervical (12.1%), ovarian (6.9%), and lung (4.9%) cancers. [5] India has the third-highest cancer burden globally, following China and the USA, with an estimated 1.4 million cases in 2015. [5] Because effective early detection methods are lacking, cancer is often diagnosed at an advanced, inoperable stage. Chemotherapy remains a key treatment strategy for improving prognosis and survival. [6] However, patients often cite chemotherapy-induced nausea and vomiting (CINV) as a major concern. [3] Despite

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improvements in antiemetic medications, CINV remains a common and feared side effect, significantly impacting quality of life, increasing healthcare costs, and hindering treatment adherence. [4] In many cases, CINV leads to adjustments or discontinuation of the primary chemotherapy regimen. This not only increases the financial burden but can also cause life-threatening complications such as dehydration, electrolyte imbalances, malnutrition, anorexia, weight loss, weakness, sleep deprivation, and even oesophageal damage and severe hemorrhage. [6]

While antiemetics like 5HT3 antagonists (e.g. Palonosetron) and NK1 receptor antagonists (e.g. Aprepitant) have improved CINV management [7], their high cost often precludes their use in standard antiemetic regimens. [6] The National Comprehensive Cancer Network (NCCN) in 2014 recommended a regimen including Olanzapine, an atypical antipsychotic, which has demonstrated superior efficacy, particularly against delayed nausea, compared to standard Aprepitant-based regimens. This Olanzapine-based approach is especially relevant for developing countries like India. However, many oncologists remain unaware of Olanzapine's potential for CINV prevention. [6]

Our government hospital frequently treats cancer patients undergoing highly emetogenic, cisplatin-based chemotherapy. While our standard antiemetic regimen of Granisetron and Dexamethasone effectively controls acute vomiting, it often fails to prevent delayed nausea. Therefore, this study will investigate the effectiveness of adding Olanzapine to our current treatment protocol for CINV prevention. We hypothesize that replacing NK-1 receptor antagonists with Olanzapine may be the most effective and affordable approach to preventing CINV. [8]

MATERIALS AND METHODS

Research design- The present study is a randomized double-blind prospective comparative study conducted for 1 year from June 2019 to May 2020 and each patient after enrolment was monitored for 4 days after initiation of therapy at Government General Hospital in collaboration with the Radiotherapy Department affiliated to Rangaraya Medical College, East Godavari district, Andhra Pradesh, India. Participants who attended the hospital for the treatment of cancer with highly emetogenic cisplatin-based chemotherapy were enrolled in the study. These patients were histologically, radiologically as well as clinically diagnosed with carcinoma of various organs.

Inclusion criteria- Patients of either sex with age above 18 years who were histologically, radiologically as well as clinically diagnosed with carcinoma and scheduled to receive cisplatin-based chemotherapy were included.

Exclusion criteria- This study excluded those patients with nausea or vomiting in the 24 hrs before the enrolment, with a known history of CNS disease (Eg: Brain metastasis or seizure disorder), on treatment with antipsychotic agents within 30 days before enrolment.

Of 125 patients screened, 32 were ineligible and 11 declined participation, resulting in 82 enrolled patients (49 women, 33 men). Participants were randomly assigned to two groups (A and B) using a computer-generated randomization tool (https://www.randomizer.org/). Patients who were non-compliant with the study medication or lost to follow-up were excluded from the final analysis. Group A received the standard treatment (Granisetron 3mg IV and Dexamethasone 16mg IV) plus Olanzapine 10mg orally, from the day before chemotherapy to day 3 post-chemotherapy. Group B received the standard treatment plus a matching placebo (manufactured by Hetero Pharmaceuticals Pvt Ltd). Both groups received their assigned medications for five days, during which daily follow-up assessments were conducted, including CINV history, other relevant parameters, compliance, and adverse effects.

Statistical Analysis- At the end of the study, blinding was disclosed. The data were expressed as Mean±SD. Results were analyzed within the group and between 2 groups using paired and unpaired t-tests with the help of SPSS software (version 20). The analysis was started when the last patient completed the total study period. The $p<0.05$ was considered statistically significant.

Ethical Approval- The study has been approved by the Institutional Ethics Committee of the hospital.

RESULTS

Out of 125 screened patients, 32 were excluded, and 11 declined participations. The remaining 82 were

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randomized 1:1 into Group A (olanzapine 10mg) and Group B (placebo), with 41 patients per group. Treatment lasted five days, starting before chemotherapy. Blinding was maintained until analysis. Five patients were lost to follow-up, leaving 77 for final analysis (Group A: 39, Group B: 38). CINV was assessed using the MASCC Antiemesis Tool and Verbal Rating Scale. Significantly more patients in the olanzapine group reported no clinically significant nausea in the early (77% vs. 42%, p=0.001), later (51% vs. 21%, p=0.005), and overall periods (46% vs. 18%, p=0.008) (Table 1).

Table 1: Primary end-point comparison between two groups

Variable	Olanzapine (N=39) No/total no (percent)	Placebo (N=38) No/total no (percent)	Group A Mean±SD	Group B Mean±SD	p-value	95% confidence interval	
						Lower limit	Upper Limit
0–24 hr after Chemotherapy							
No nausea	30/39 (76.9%)	16/38 (42.1%)	1.77±0.43	1.42±0.50	0.001	0.14	0.56
25–120 hr after Chemotherapy							
No nausea	20/39 (51.2%)	8/38 (21%)	1.51±0.51	1.21±0.41	0.005	0.09	0.51
0–120 hr after chemotherapy							
No nausea	18/39 (46.1%)	7/38 (18.4%)	1.46±0.51	1.18±0.39	0.008	0.07	0.48

A significantly greater proportion of patients in the olanzapine group achieved a complete response compared to the placebo group across all assessment periods. Specifically, this was observed during the early period (87% vs. 55%, p=0.001), the later period (71% vs. 47%, p=0.029), and overall (66% vs. 34%, p<0.004) (Table 2).

Table 2: Secondary endpoint- Complete response comparison between two groups

Variable	Olanzapine (N=39) No/Total (%)	Placebo (N=38) No/Total (%)	Group A Mean±SD	Group B Mean±SD	p-value	95% confidence interval	
						Lower Limit	Upper Limit
0–24 hr after chemotherapy							
No vomiting/ CR	34/39 (87.1%)	21/38 (55.3%)	1.87±0.34	1.55±0.50	0.001	0.12	0.51
25–120 hr after chemotherapy							
No vomiting / CR	28/39 (71.8%)	18/38 (47.3%)	1.72±0.46	1.47±0.51	0.029	0.03	0.46
0–120 hr after chemotherapy							
No vomiting / CR	26/39 (66.6%)	13/38 (34.2%)	1.67±0.48	1.34±0.48	0.004	0.11	0.54

In Fig. 1, the bar chart compares the percentage of patients experiencing no nausea in the olanzapine and placebo groups over different periods. Olanzapine significantly reduced nausea, with higher rates of no nausea at 0-24 hours (76.9% vs. 42.1%), 25-120 hours (51.2% vs. 21%), and overall (46.1% vs. 18.4%).

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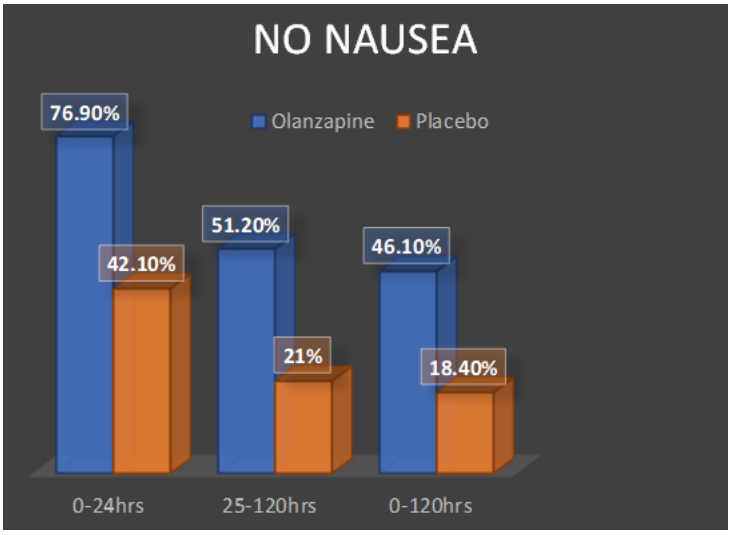

Fig. 1: Bar diagram showing percentage of patients with no nausea in both groups

This chart illustrates the percentage of patients with no vomiting or complete response in both groups. The olanzapine group showed superior outcomes at 0-24 hours (87.1% vs. 55.3%), 25-120 hours (71.8% vs. 47.3%), and overall (66.6% vs. 34.2%), indicating a significant benefit in controlling chemotherapy-induced vomiting (Fig. 2).

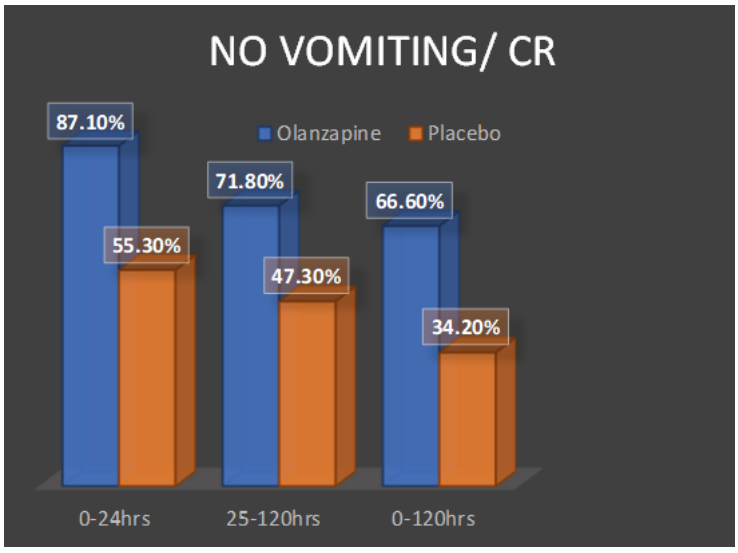

Fig. 2: Bar diagram showing the percentage of patients with no Vomiting or Complete Response

MASCC Antiemesis Tool (MAT) was used to assess post-chemotherapy nausea intensity and vomiting frequency in both Group A and Group B. Unpaired t-tests revealed a statistically significant difference ($p<0.05$) between the two groups, indicating that olanzapine was more effective in reducing chemotherapy-induced nausea and vomiting (CINV) (Tables 3 & 4).

Table 3: Nausea Intensity score (MAT) comparison between two groups

	CINV period	Group A Mean±SD	Group B Mean±SD	p-value	95% confidence interval	
					Lower limit	Upper Limit
Nausea Intensity score	0-24hrs	5.22±1.09	7.77±1.02	0.0001	-3.39	-1.71
	25-120hrs	2.75±1.02	7.25±0.93	0.0001	-5.06	-3.93
	0-120hrs	2.22±1.18	6.47±1.85	0.0001	-5.12	-3.36

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Table 4: Comparison of frequency of vomiting between both groups

	CINV period	Group A Mean±SD	Group B Mean±SD	p-value	95% confidence interval	
					Lower limit	Upper Limit
Frequency of Vomiting	0-24hrs	1.40±0.55	3.24 ±0.56	<0.0001	-2.43	-1.24
	25-120hrs	3.18±1.66	10.65±2.70	<0.0001	-9.31	-5.63
	0-120hrs	3.50±2.15	12.29±3.94	<0.0001	-11.31	-6.27

Both treatment groups tolerated their assigned medications well, experiencing only minor side effects that did not lead to treatment discontinuation. Adverse events were reported in 16 of the 39 patients (41%) in the olanzapine group (Group A) and 4 of the 38 patients (10%) in the placebo group (Group B) (Table 5). Patients receiving olanzapine experienced increased sedation on Day 2 compared to baseline, but this was resolved by Days 3, 4, and 5, despite continued administration of the drug.

Table 5: The safety profile of two intervention groups

Adverse Events	Group A		Group B	
	N	%	N	%
Undesired sedation	12	30.7	4	10
Undesired increase in appetite	4	10.2	0	0

In Group A (n=39), of the 16 patients experiencing side effects, the most common was undesired sedation (12 patients, 30%), followed by undesired increased appetite (4 patients, 10%). In Group B (n=38), all 4 patients (10%) with side effects experienced undesired sedation.

DISCUSSION

Several studies support adding Olanzapine to a 5HT3 antagonist plus dexamethasone regimen for CINV prevention in patients receiving highly emetogenic chemotherapy. While numerous drugs exist for managing acute nausea and vomiting, delayed nausea and vomiting (occurring more than 24 hours after chemotherapy) remains a significant challenge. This study evaluated the effectiveness of Olanzapine as an add-on therapy compared to placebo, focusing on its impact on nausea and vomiting during the early, delayed, and overall assessment periods [9,10].

Our results demonstrated that in Group A, repetitive doses of Olanzapine along with standard treatment effectively reduced both acute and delayed nausea and vomiting from day 0 to day 4, and showed statistically significant results when compared with Group B where repeated doses of Placebo along with standard treatment were given. Whereas tolerability wise Olanzapine group has shown few adverse effects compared to the Placebo group.

Several studies have explored the use of olanzapine for CINV. Navari *et al.* [11] reported similar efficacy and safety profiles for olanzapine, although their study used palonosetron instead of the granisetron used in the present study. Tan *et al.* [12] also found olanzapine effective, improving both efficacy and quality of life, but their study lacked a placebo control and included patients receiving both high and moderately emetogenic chemotherapy. Seeman [13] investigated olanzapine in patients with refractory CINV across all chemotherapy emetogenicity levels, concluding that it significantly improved overall CINV control even when prior prophylactic and breakthrough antiemetics had failed [14].

A 2016 systematic review and meta-analysis by Navari *et al.* [15] investigated Olanzapine's effectiveness in preventing and treating CINV. They searched Ovid MEDLINE (1946-June 2015), EMBASE and EMBASE Classic (1947-June 2015), and the Cochrane Central Register of Controlled Trials (up to June 2015), identifying 13 relevant randomized controlled trials (RCTs). Ten RCTs examined preventative Olanzapine use, involving 546 patients receiving Olanzapine and 536 receiving other 5-HT3 or NK1 receptor antagonists [16,17]. Three RCTs explored Olanzapine as rescue therapy for breakthrough CINV, with 120 patients receiving Olanzapine and 188 receiving other rescue antiemetics. In the rescue setting, the meta-analysis found Olanzapine statistically superior

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in preventing emesis, the only endpoint available for analysis.

CONCLUSIONS

Olanzapine significantly outperformed placebo in preventing nausea and improving the complete response rate for CINV in chemotherapy-naive patients receiving highly emetogenic chemotherapy (HEC). Over a decade of research, including case reports, retrospective analyses, and phase I-III clinical trials, has consistently demonstrated Olanzapine's efficacy in preventing CINV and treating both breakthrough and refractory CINV, with a low incidence of severe adverse reactions. It has also shown superior efficacy compared to aprepitant and dexamethasone, especially in managing delayed nausea and vomiting. These results justify further investigation into Olanzapine's potential.

CONTRIBUTION OF AUTHORS

Research concept- Krishna Sai Attili, Hemanth Kumar Bura

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Data collection- Krishna Sai Attili, Vineela Ganta

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Literature search- Hemanth Kumar Bura, Krishna Sai Attili

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Article editing- Krishna Sai Attili, Hemanth Kumar Bura

Final approval- Usha Kiran Prayaga, Mendu Swetha Bindu

REFERENCES

[1] Mallath MK, Taylor DG, Badwe RA, Rath GK, Shanta V, Pet al. The growing burden of cancer in India: epidemiology and social context. Lancet Oncol., 2014; 15(6): e205-12.

[2] World Health Organization. Cancer. Updated on 3 February 2025. Available at: https://www.who.int/news-room/fact-sheets/detail/cancer.

[3] Osoba D, Zee B, Warr D, Latreille J, Kaizer L, Pater J. Effect of postchemotherapy Nausea and Vomiting on health-related quality of life. Support Care Cancer, 1997; 5(4): 307-13.

[4] Rao KV, Faso A. Chemotherapy-induced nausea and Vomiting: optimizing prevention and management. Am Health Drug Benefits, 2012; 5(4): 232.

[5] Mathew A, George PS, KM JK, Vasudevan D, James FV. Transition of cancer in populations in India. Cancer Epidemiol., 2019; 58: 111-20.

[6] Wang SY, Yang ZJ, Zhang L. Olanzapine for preventing Nausea and Vomiting induced by moderately and highly emetogenic Chemotherapy. Asian Pac J Cancer Prev., 2014; 15(22): 9587-92.

[7] Chow R, Chiu L, Navari R, Passik S, Chiu N, et al. Efficacy and safety of olanzapine for the prophylaxis of chemotherapy-induced nausea and vomiting (CINV) as reported in phase I and II studies: a systematic review. Support Care Cancer, 2016; 24(2): 1001-08. doi: 10.1007/s00520-015-3000-6.

[8] Yokoe T, Hayashida T, Nagayama A, Nakashoji A, Maeda H, et al. Effectiveness of Antiemetic Regimens for Highly Emetogenic Chemotherapy-Induced Nausea and Vomiting: A Systematic Review and Network Meta-Analysis. Oncol., 2019; 24(6): e347-57.

[9] Hosick HL, Rizzo C, Campanella JJ, Alder R. Magill's Medical Guide (Online Edition), 2019; pp. 5.

[10] Sutherland A, Naessens K, Plugge E, Ware L, Head K, et al. Olanzapine for the prevention and treatment of cancer-related nausea and vomiting in adults. Cochrane Database Syst Rev., 2018; 9(9): CD012555. doi: 10.1002/14651858.CD012555.pub2.

[11] Navari RM, Qin R, Ruddy KJ, Liu H, Powell SF, et al. Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting. N Engl J Med., 2016; 375(2): 134-42. doi: 10.1056/NEJMoa1515725.

[12] Tan L, Liu J, Liu X, Chen J, Yan Z, et al. Clinical research of Olanzapine for prevention of chemotherapy-induced Nausea and Vomiting. J Exp Clin Cancer Res., 2009; 28(1): 131.

[13] Seeman P. Atypical antipsychotics: mechanism of action. Can J Psychiatry., 2002; 47(1): 27-38.

[14] Haiderali A, Menditto L, Good M, Teitelbaum A, Wegner J. Impact on daily functioning and indirect/direct costs associated with chemotherapy-induced Nausea and Vomiting (CINV) in a US population. Supportive Care Cancer, 2011; 19(6): 843-51.

doi: 10.21276/SSR-IIJLS.2025.11.1.30

[15]Navari RM, Gray SE, Kerr AC. Olanzapine versus Aprepitant for the prevention of chemotherapy-induced Nausea and Vomiting: a randomized phase III trial. J Supportive Oncol., 2011; 9(5): 188-95.doi: 10.1016/j.suponc.2011.05.002.

[16]Hesketh PJ. Chemotherapy-induced Nausea and Vomiting. New England J Med., 2008; 358: 2482-94.

[17]Adel N. Overview of chemotherapy-induced Nausea and Vomiting and evidence-based therapies. Am J Managed Care, 2017; 23(14 Suppl): S259-65.