Article published online: 2025-09-25

THIEME OPEN ACCESS

Olanzapine versus Aprepitant for Prophylaxis of Nausea and Vomiting in Patients Receiving Highly Emetogenic Chemotherapy: A Prospective Randomized Study

Lakshmi D. Gedela[1] Rachana Chennamaneni[2] Konatam Meher Lakshmi[2] Stalin Chowdary Bala[3] Sadashivudu Gundeti[2]

[1] Department of Medical Oncology, Konaseema Institute of Medical Sciences, Amalapuram, Andhra Pradesh, India
[2] Department of Medical Oncology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India
[3] Department of Medical Oncology, Mahatma Gandhi Cancer Institute, Visakhapatnam, Andhra Pradesh, India

Address for correspondence Rachana Chennamaneni, DM, Department of Medical Oncology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad 500082, Telangana, India (e-mail: rachanarajch@gmail.com).

Ind J Med Paediatr Oncol

Abstract

Introduction Chemotherapy-induced nausea and vomiting (CINV) negatively affects health-related quality of life and performance status in patients undergoing chemotherapy. Aprepitant, palonosetron, and steroids (APD) notably enhance the rates of complete response (CR) in patients receiving highly emetogenic chemotherapy (HEC). This study compares the efficacy, cost, and quality of life between APD and olanzapine, palonosetron, and dexamethasone (OPD).

Objectives The main aim of the study was to evaluate the control of CINV by measuring CR and total control (TC). The secondary aim was to examine the impact of CINV on patients' quality of life.

Materials and Methods This is a prospective randomized study of patients newly diagnosed with malignancy, aged > 18 years. This analysis was done over a period of 1 year in patients receiving HEC. All patients eligible for the study are randomized to APD versus OPD regimen. Stratification was done according to the chemotherapy regimen used. Quality of life, the secondary objective, was assessed by using the Functional Living Index-Emesis.

Results Overall, 120 patients were randomized during the study period to both the arms at 1:1 ratio. Baseline characteristics were equally matched between both the arms. Both the arms showed effective prevention of vomiting in nearly 80% of the study population. Emesis was reported in 19% of APD and 20% in the OPD arm ($p = 0.75$). Grade 3/4 vomiting was not seen in any patient in the olanzapine group. The CR rates in all patients are 75 and 77% with APD and OPD arms, respectively ($p = 0.83$). Overall, the TC of CINV is similar among the two groups, 57 and 60% in APD and OPD, respectively ($p = 0.85$). Delayed nausea was significantly lower in the OPD arm compared with APD (17% vs. 38%, respectively, $p = 0.025$). In patients receiving anthracycline plus

Keywords
- aprepitant
- olanzapine
- highly emetogenic chemotherapy
- nausea and vomiting

DOI https://doi.org/10.1055/s-0045-1811936.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

cyclophosphamide chemotherapy, OPD outperformed APD in delayed nausea and delayed TC ($p = 0.002$ and 0.015, respectively). Both drugs were effective in maintaining a good quality of life and no significant difference was observed among both the groups. The most common toxicity observed in both the arms was anorexia.

Conclusion Both regimens had similar efficacy in preventing CINV, with no significant differences in CR and TC rates. Olanzapine was more effective for delayed nausea than aprepitant, suggesting it is a cost-efficient alternative for managing CINV in HEC patients.

Introduction

Maintaining good health-related quality of life (QOL) and performance status is essential for individuals undergoing chemotherapy. This is negatively affected by chemotherapy-induced nausea and vomiting (CINV).[1] Chemotherapy-induced nausea is the most distressing adverse effect, affecting approximately two-thirds of patients receiving chemotherapy regimens, that are moderately or highly emetogenic. This is in spite of extensive application of antiemetic therapies.[2,3]

The combination of neurokinin receptor 1 antagonist, aprepitant, and a second-generation serotonin (5-HT3) receptor antagonist, palonosetron, in conjunction with corticosteroids, has shown a notable enhancement in complete response (CR) rates among those undergoing highly emetogenic chemotherapy (HEC). The inclusion of aprepitant resulted in CR in nearly two-thirds of the patients during both acute and delayed phase of emesis, better control during the acute phase, representing a significant advancement compared with prophylactic regimens that did not include aprepitant.[4–6] Antiemetic studies that analyzed rates of nausea as an endpoint, have shown poor control of nausea with current antiemetic regimens.[7] Although these regimens have substantially decreased the incidence of CINV, majority still continue to experience these adverse events, particularly nausea. This underscores the necessity for a deeper understanding of the underlying pathophysiology and the exploration of novel therapeutic options that can more effectively manage CINV, thereby enhancing patients' treatment adherence by maintaining QOL.[8]

A second-generation atypical antipsychotic, olanzapine, has been evaluated for its impact on managing CINV. Its antiemetic properties are believed to stem from its antagonistic effects on the dopamine (D2) and serotonin (5-HT2C and 5-HT3) receptors. Numerous clinical trials have demonstrated that regimens that incorporate olanzapine along with a 5-HT3 receptor antagonist and corticosteroids enhance the control of nausea in patients undergoing chemotherapy which is moderately to highly emetogenic.[9–11] Several clinical trials have compared three-drug regimens incorporating either olanzapine or aprepitant which revealed comparable CR rates among both the regimens. However, olanzapine has demonstrated superior complete control rates, particularly in preventing CINV in the delayed phase.

This study aims to compare the efficacy, cost of antiemetic regimen, and impact on QOL associated with the use of aprepitant, palonosetron, and dexamethasone (APD) against the olanzapine, palonosetron, and dexamethasone (OPD) regimen.

Materials and Methods

Study Design

This is a prospective, randomized control study conducted in our department over a course of 1 year.

Sample size: The study comprised of 120 patients newly diagnosed with malignancy whose treatment plan included administration of HEC.

Inclusion Criteria

All patients aged > 18 years and receiving anthracycline plus cyclophosphamide (AC) or carboplatin area under the curve ≥ 4 or cisplatin or dacarbazine are included in the study. These regimens were chosen according to the National Comprehensive Cancer Network classification of highly emetic chemotherapy regimens.[12] They should have adequate organ function and free of nausea or vomiting 24 hours prior to initiation of chemotherapy.

Exclusion Criteria

Those receiving concurrent radiation, those with brain metastasis, pregnant women or lactating women, those suffering with psychiatric disorders, or on antipsychotic medications were not included in the study. Written informed consent was taken from all the study participants before enrolment.

Primary and Secondary Objective

The primary objective of the study was to evaluate the CINV control in terms of CR and total control (TC). CR is defined as "no emetic episodes and no use of rescue antiemetic medication during the 120-hour period after the start of chemotherapy (overall period)." TC is defined as "no emetic episode, no use of rescue medication, and no nausea."

The secondary objective was to analyze the effect of CINV on patient's QOL. This was evaluated by using the Functional Living Index-Emesis (FLIE) on day 0 and day 6 of chemotherapy.

All eligible participants in the study were randomly assigned to either the OPD regimen or the APD regimen, based on a computer-generated randomization schedule developed by a statistician who is not associated with the study. Additionally, stratification was done according to their chemotherapy regimen. The patient in the APD arm received aprepitant 125 mg on day 1 and aprepitant 80 mg on day 2 and day 3 (Arm b) as part of prophylactic antiemetic therapy and those in the OPD (Arm A) arm received olanzapine 10 mg at bedtime on days 1 to 4. Patients in both groups received palonosetron at a dosage of 0.25 mg and dexamethasone at 12 mg intravenously, which were given half an hour prior to the initiation of chemotherapy on day 1. Throughout the study duration, as needed, either for nausea or vomiting patients were allowed to use rescue medication.

Demographic details of all patients are recorded. Pre-chemotherapy nausea and vomiting and QOL are recorded. The FLIE is the sole validated questionnaire specifically designed to assess the effects of CINV on patients' everyday lives. It evaluates two domains—nausea and vomiting—individual domain has nine items, with a recall period of 5 days. The responses for the 18 items are consolidated to get the final score which can range from 18 to 126. Higher scores indicate better health outcomes and a diminished effect of CINV on daily life. Impact of CINV on daily functioning is nil or negligible for a final score of 108 or above in the FLIE questionnaire.

Period of assessment of emesis was done within the first 24 hours after the administration of chemotherapy (acute chemotherapy-induced emesis) and every day from the 2nd to the 5th day after chemotherapy (delayed emesis). Distinct episodes of emesis are defined by a period of at least 1 minute without vomiting or retching.

Patients were requested to document the number and severity of emetic episodes and nausea, and they were stratified according to the Common Terminology Criteria for Adverse Events grading v.5.[13] The utilization of rescue medications (including type and dosage) and any adverse events were evaluated using a 4-point Likert scale (0—none; 1—mild; 2—moderate; 3—severe) in a daily diary maintained over a 5-day period. On day 5, patients were instructed to document the details of any health care visits related to managing nausea or vomiting that occurred in the preceding 5 days. The diaries were collected at the end of the study period. Vomiting and retching (nonproductive vomiting), collectively referred to as emesis, were quantitatively evaluated through direct observation by the subjects, by tallying the number of emetic episodes.

Statistical Analysis

GraphPad Prism software was used for all statistical analysis.[13,14] Chi-square test was conducted to test the difference in response rates between the two arms. A two-sided p-value of < 0.05 was considered significant. The QOL scores assessed by the FLIE questionnaire were represented using bar diagrams and significance between the two arms was assessed using the chi-square test.

Ethical Approval

The study was approved by Institutional Ethics Committee registered with number EC/NIMS/2447/2019 dated November 23, 2019. All procedures performed in this study involving human participants complied with the ethical standards established by the institutional and/or national research committees, as well as the principles outlined in the 1964 Helsinki Declaration and its subsequent amendments or equivalent ethical guidelines.

Results

A total of 122 patients planned to receive HEC during the study period were included and were randomized into two study groups: APD and OPD (►**Fig. 1**).

Sixty patients were randomized to each group. The median age was 50 years (range: 19–70 years). Majority of patients were females with a sex ratio of 7:1. Fifty-seven (95%) and 58 (96%) had performance status of ≤ 1 in the APD and OPD groups, respectively. Thirteen (21%) and 18 (30%) patients in the APD and OPD group, respectively, had comorbidities at the time of randomization, the most common being hypertension. The most common regimen in both groups is AC in 56 (47%) patients. The next common regimens in the study population are paclitaxel and carboplatin in 38 (32%), followed by cisplatin in 14 (11%) and dacarbazine in 12 (10%). Baseline characteristics are outlined in ►**Table 1**.

Nausea was reported in 40% of APD and 33% in the OPD arm ($p = 0.361$). Acute and delayed nausea was reported in 32 and 38% patients in APD and 30 and 17% in OPD arms ($p = 0.37$ and $p = 0.025$), respectively. Grade 1 and 2 nausea was 26 and 6% in the APD arm and 28 and 2% in the OPD arm, respectively.

Both the arms showed effective prevention of vomiting in nearly 80% of the study population. Emesis was reported in 19% of APD and 20% in the OPD arm ($p = 0.75$). Acute and delayed emesis and grade is shown in ►**Fig. 2**. Grade 3/4 emesis was not seen in any patient in the olanzapine group. Only one patient in the aprepitant group had grade 3 emesis.

The CR rates in acute phase are 78 and 85% in the APD and OPD arms, respectively, with $p = 0.47$. In delayed phase, the CR rates were 82% in both the study groups ($p = 1$). The CR rates in all patients are 75 and 77% with the APD and OPD arms, respectively ($p = 0.83$) (►**Fig. 3**).

The TC rates in acute phase are 60 and 65% in the APD and OPD arms, respectively ($p = 0.7$). In delayed phase the TC rates are 58 and 73% in the APD and OPD arms, respectively ($p = 0.123$). Overall, the TC of CINV is similar among the two groups, 57 and 60% in APD and OPD, respectively ($p = 0.85$) (►**Fig. 4**).

Subgroup analyses were done based on the type of chemotherapy received (►**Table 2**). In patients receiving AC chemotherapy, APD is equal to OPD in CR, TC, and acute TC. OPD is superior to APD in delayed nausea and delayed TC ($p = 0.002$ and 0.015, respectively). In patients receiving carboplatin-based chemotherapy, both drugs are equal in efficacy and provided CR rates of more than 85%. The number of patients in our study receiving cisplatin-based and

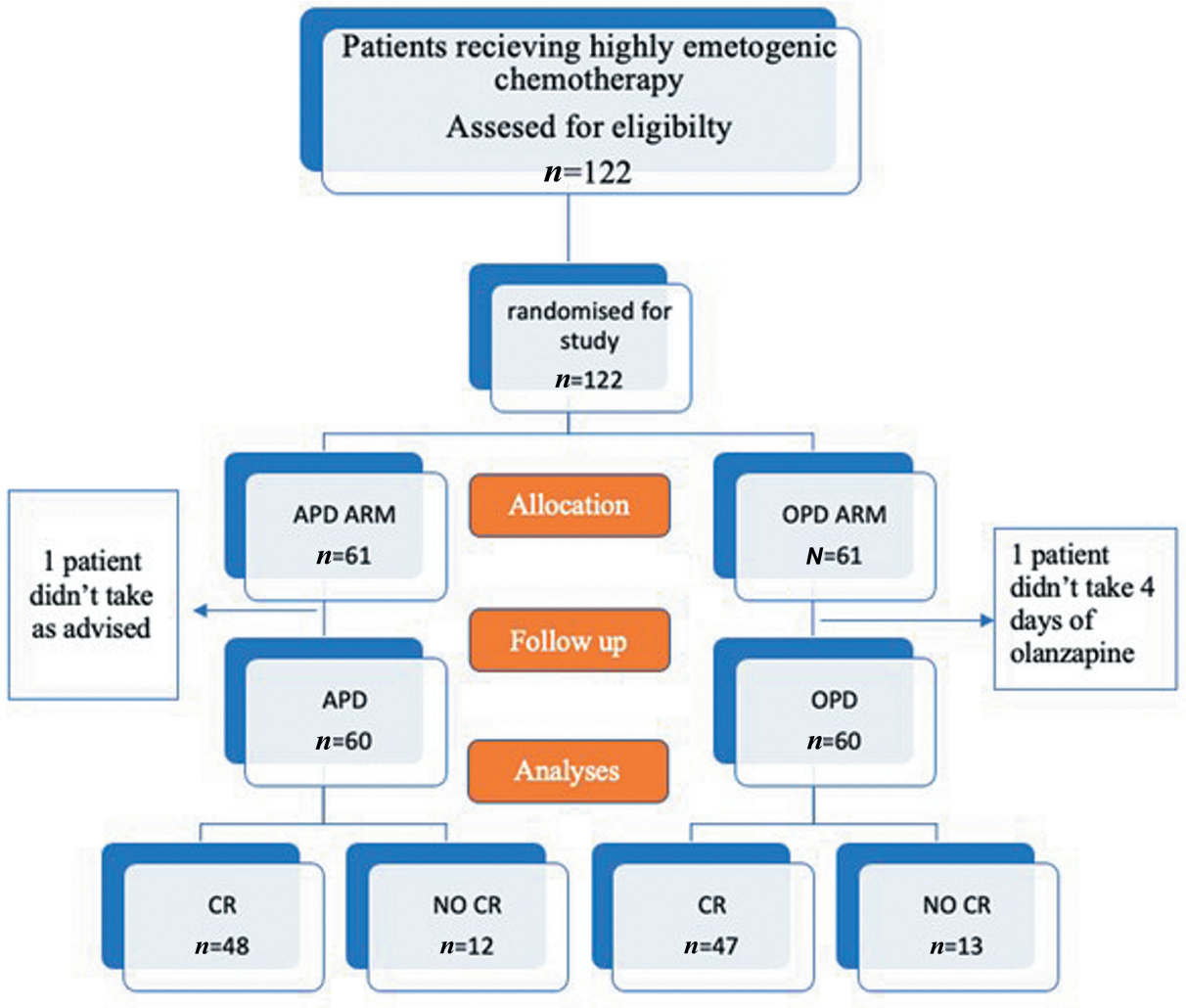

Fig. 1 Consort diagram.

dacarbazine-based regimens was very few so efficacy analysis could not be done between the two arms.

Only 11 (9%) patients of the entire study population required the usage of rescue medication. Around 8 (13%) patients in the APD group and 3 (5%) in the OPD group required rescue medication ($p = 0.201$). The drugs used are domperidone and metoclopramide.

No variation was observed in QOL between both the study arms and both drugs were effective in maintaining a good QOL. FLIE score was > 108 in 80 and 83% in the APD and OPD study groups, respectively. Inability to enjoy meal was the most common problem patients faced due to nausea in both study groups with composite score of 5.8 and 6.2 in the APD and OPD arms, respectively. Inability to enjoy meal and make meals or do tasks was the most common problem patients faced due to vomiting in both the study groups. The least affected component in both the study arms was daily functioning due to vomiting with a composite score of 6.8 and 6.9 in the APD and OPD arms, respectively.

The most frequently observed toxicity in both the arms was anorexia (50 and 52% in the APD and OPD arm, respectively). Thirty (50%) patients in the OPD arm had drowsiness, which was significantly higher compared with 5% in the APD arm ($p = 0.0001$). All other side effects observed were similar among the two groups and none were statistically relevant. The adverse effects seen in the APD and OPD groups are as depicted in ►**Table 3**.

Discussion

Despite advancements in its prevention, CINV remains one of the most feared adverse effects of cancer chemotherapy. Poorly managed CINV can result in reduced QOL, treatment delays, dosage reductions, the need for additional antiemetic prophylaxis, increased pressure on health care resources, and even early termination of chemotherapy.

The antipsychotic medication olanzapine has demonstrated its effectiveness as prophylaxis against both acute and delayed CINV in patients undergoing moderately emetogenic chemotherapy to HEC, as evidenced by various phase 1 and 2 studies.[9,15] This drug was also compared with aprepitant by Navari et al and Tan et al in prospective randomized control studies, which showed that there is similar vomiting control and superior nausea control with olanzapine.[16,17]

In a developing country like India, where the majority of patients are from low-income group, the cost of therapy

Table 1 Baseline demographic characteristics

Characteristic	APD (%)	OPD (%)	Total (%)
Number of patients (*n*)	60 (50)	60 (50)	120
Median age (range) in years	48 (19–70)	54 (19–80)	50 (19–80)
Sex			
Male Female	7 (12) 53 (88)	7 (12) 53 (88)	14 (12) 106 (88)
ECOG PS			
0 1 2	10 (17%) 47 (78%) 3 (5)	7 (12) 51 (85) 2 (3)	17 (14) 98 (82) 8 (4)
Comorbidities			
None Diabetes Hypertension Diabetes and hypertension Hypothyroid Others	47 (78) 2 (3) 4 (7) 2 (3) 4 (7) 1 (2)	42 (70) 3 (5) 6 (10) 6 (10) 1 (2) 2 (3)	89 (74) 5 (4) 10 (8) 8 (7) 5 (4) 3 (3)
Primary malignancy			
Breast Ovary Osteosarcoma Hodgkin lymphoma	28 (47) 19 (31) 7 (12) 6 (10)	28 (47) 20 (33) 6 (10) 6 (10)	56 (47) 39 (32) 13 (11) 12 (10)

Abbreviations: APD, aprepitant, palonosetron, and dexamethasone; ECOG PS, Eastern Cooperative Oncology Group Performance Status; OPD, olanzapine, palonosetron, and dexamethasone.

plays a major role in maintaining proper compliance to therapy. Olanzapine becomes an economically viable alternate medication to such a population to complete the planned chemotherapy.

The primary objective of the study was to achieve a CR during the overall phase of chemotherapy. The study demonstrated that both drugs provided an equivalent rate of CR over the 5-day observation period in the two randomized groups, confirming their equal efficacy in preventing CINV. Study by Babu et al showed similar findings whereas that by Navari et al showed superior CR rates with olanzapine.[16,18] A network meta-analysis done comparing various antiemetic regimens had also shown that both regimens are of equal efficacy with odds ratio of 1.16 (*p*-value: 0.46), 2.13 (*p*-value: 0.06), and 1.27 (*p*-value: 0.25) in overall, acute, and delayed phases, respectively.[19] The CR rates during the acute and delayed phases with aprepitant and olanzapine were found to be equivalent, indicating that both medications possess similar efficacy in preventing CINV in both phases.

The TC rates with aprepitant and olanzapine are 60, 58, and 57% and 65, 73, and 60%, respectively, in acute, delayed, and overall phases. There is no statistically meaningful difference between both the drugs. This is the first randomized study to report TC rates in aprepitant and olanzapine arms.

Prevention of nausea was successful in 60% patients in the APD regimen and 67% in the OPD arm during the overall study period, though the numerically higher difference was not significant at the statistical level. In the acute phase, the nausea control with olanzapine and aprepitant was similar. Nausea control in delayed phase was superior with olanzapine in our study like that seen in the analysis by Navari et al.[16] Olanzapine demonstrated superior efficacy over aprepitant in the delayed phase, likely due to its unique mechanism of action, which targets various receptors within the CINV pathway. Among patients who experienced nausea, 83% in the aprepitant arm and 95% in the olanzapine arm reported only grade 1 nausea.

The emesis control rates in the APD arm are 83% in acute, 82% in delayed, and 82% in overall phases. With olanzapine, the emesis control rates are 87% in acute, 82% in delayed, and 80% in overall phases. Aprepitant and olanzapine were similar in terms of preventing vomiting, like the study by Babu et al.[18] Grade 1 is the most common toxicity grade for vomiting like that of nausea in this study. In the meta-analysis by Sarma et al, similar results of better nausea control in overall phase with olanzapine and comparable emetic control across treatment arms was reported.[20]

AC chemotherapy is classified as one of the highly emetogenic regimens frequently employed in the treatment of the most prevalent cancer among women. In this study, a statistically significant enhancement in nausea control and delayed TC rates was noted in the olanzapine arm compared with the aprepitant arm. These results are similar to the study done by Shivaprakash et al except for the significant benefit with olanzapine seen in delayed nausea control.[21] In their study, there was no delayed nausea or vomiting in either arm. The olanzapine arm had a higher proportion of patients who experienced no nausea or vomiting compared with the aprepitant arm; however, this difference was not statistically relevant.

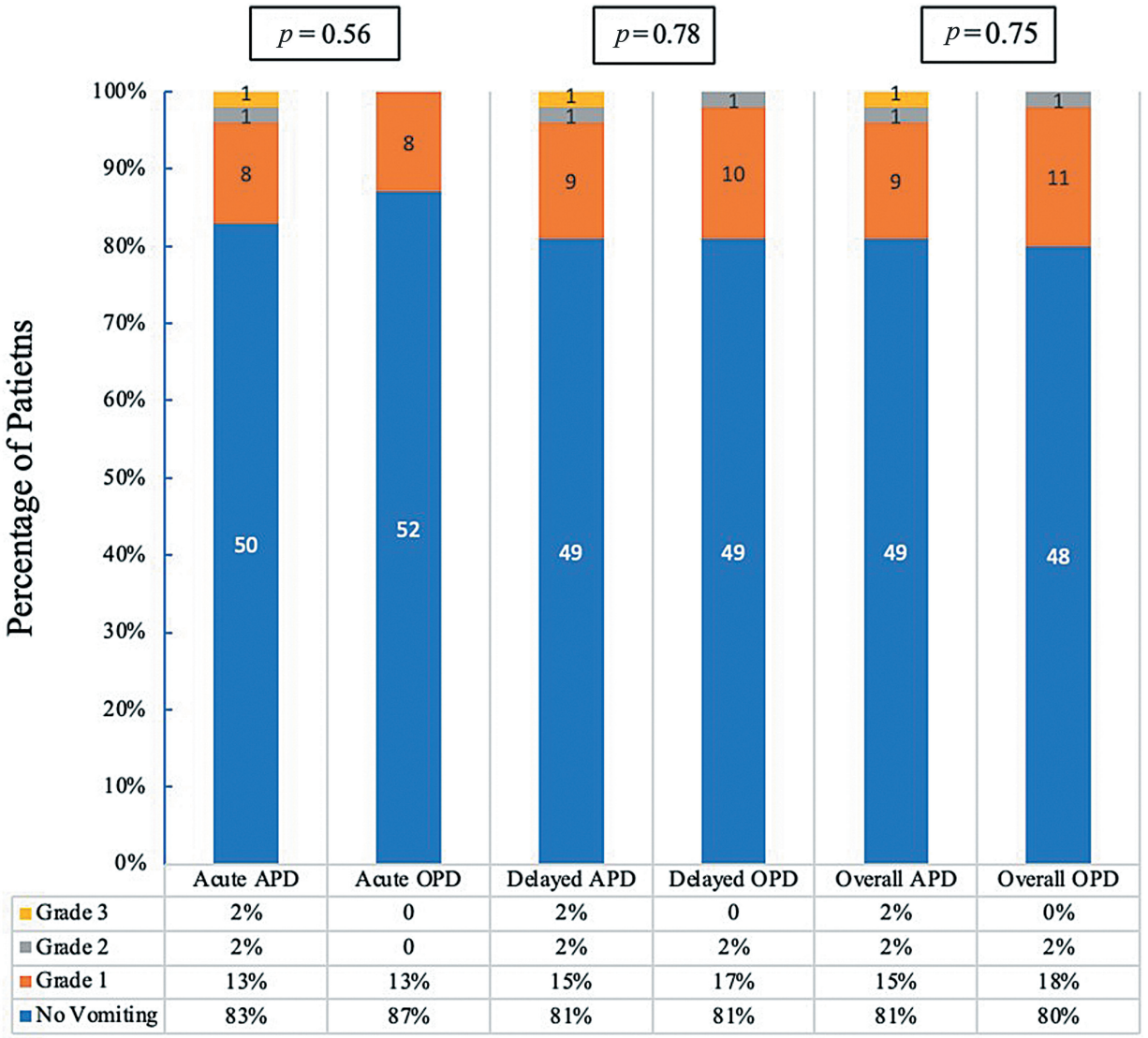

Fig. 2 Incidence and severity of emesis.

Research has demonstrated that despite receiving antiemetic therapy, patients' QOL may still be negatively affected by CINV.[22] In our study, on day 6 post-chemotherapy, the mean total FLIE scores were 118 in the APD arm and 120.13 in the OPD arm. Approximately 80% of patients in the APD group and 83% in the OPD group

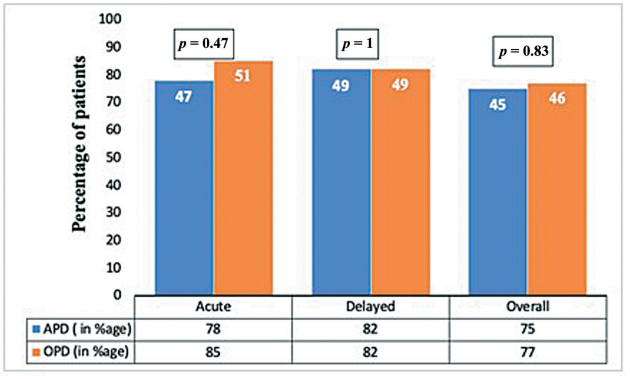

Fig. 3 Complete response in acute, delayed, and overall phases with aprepitant and olanzapine prophylaxis in patients receiving highly emetogenic chemotherapy (HEC).

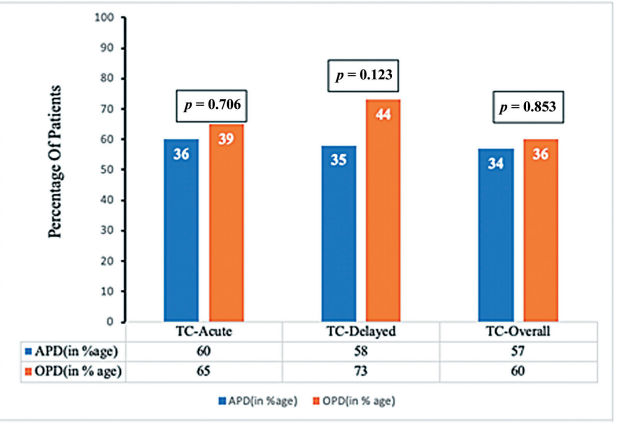

Fig. 4 Total control in acute, delayed, and overall phases of highly emetogenic chemotherapy with aprepitant and olanzapine prophylaxis.

Table 2 Emesis response based on the chemotherapy regimen in aprepitant and olanzapine arms

	AC			Carboplatin		
	APD ($n = 28$) (%)	OPD ($n = 28$) (%)	*p*-Value	APD ($n = 19$) (%)	OPD ($n = 20$) (%)	*p*-Value
No nausea						
Acute	15 (55)	19 (68)	0.411	18 (95)	15 (75)	0.206
Delayed	12 (43)	24 (86)	0.002	18 (95)	18 (90)	0.57
Overall	11 (39)	19 (68)	0.06	18 (95)	15 (75)	0.206
No vomiting						
Acute	21 (75)	24 (86)	0.501	18 (95)	17 (85)	0.63
Delayed	21 (75)	22 (79)	0.75	18 (95)	17 (85)	
Overall	21 (75)	22 (79)	0.75	18 (95)	17 (85)	
CR						
Acute	18 (64)	24 (86)	0.122	18 (95)	17 (85)	0.63
Delayed	21 (75)	22 (79)	0.75	18 (95)	17 (85)	0.63
Overall	18 (64)	22 (79)	0.374	18 (95)	16 (80)	0.36
TC						
Acute	10 (36)	16 (57)	0.18	18 (95)	15 (75)	0.206
Delayed	10 (36)	20 (71)	0.015	18 (95)	17 (85)	0.63
Overall	9 (32)	15 (54)	0.177	18 (95)	15 (75)	0.206

Abbreviations: AC, anthracycline plus cyclophosphamide; APD, aprepitant, palonosetron, and dexamethasone; CR, complete response; OPD, olanzapine, palonosetron, and dexamethasone; TC, total control.

reported that CINV had nil or negligible impact on their daily life, defined as a total FLIE score greater than 108, with no statistically meaningful difference observed between both the groups. When individual components in the nausea and vomiting domain were compared, it was seen that inability to enjoy meals due to nausea mainly contributed to impaired QOL. Consequently, nausea was found to exert a more pronounced negative effect on QOL compared with vomiting. Olanzapine-based regimens may facilitate greater improvements in QOL due to their superior efficacy in controlling nausea compared with aprepitant.

The side effects that were common with aprepitant were anorexia, headache, and fatigue. The side effects seen more with olanzapine were drowsiness, anorexia, and fatigue. Only drowsiness was significantly more with olanzapine compared with the aprepitant arm. It was only grade 1 and grade 2 in some patients without affecting daily activities. Cancer patients usually suffer from insomnia due to anxiety and disease-related pain and fatigue. This side effect of olanzapine is a blessing in disguise as it helps the patient to get through the day by providing adequate sleep and rest. Hence, the adverse effect of olanzapine should not preclude the clinician from using the drug but should be considered advantageous to the patient. Hypotension was seen in one patient in the aprepitant arm and two patients in the olanzapine arm. This was consistent with the toxicities observed in previous studies.[17,22,23] In both the arms, no grade 3 or 4 toxicities were observed.

Table 3 Adverse effects experienced by the study population with aprepitant and olanzapine

Toxicity	APD	OPD	*p*-Value	
	Grade 1/2	Grade 1/2		Grade ¾ Both arms
Drowsiness	3 (5%)	30 (50%)	0.0001	0
Extrapyramidal	0	0	1	0
Hypotension	1 (2%)	2 (3%)	1	0
Headache	23 (38%)	14 (23%)	0.113	0
Fatigue	22 (37%)	19 (32%)	0.70	0
Hiccups	1 (2%)	1 (2%)	1	0
Constipation	15 (25%)	17 (28%)	0.83	0
Diarrhea	3 (5%)	5 (8%)	0.717	0
Anorexia	30 (50%)	31 (52%)	1	0

Abbreviations: APD, aprepitant, palonosetron, and dexamethasone; OPD, olanzapine, palonosetron, and dexamethasone.

Most patients in our institute belong to the low-income group where treatment is offered with the aid of government-sponsored schemes. Affordability is a major hurdle in treatment completion for patients who do not have proper resources. Spending more on antiemetic therapy would make it even more difficult in treatment completion. Availability of less expensive alternatives would make a huge impact in the overall budget of treatment. In our country, the price of aprepitant per cycle is 20 times more than that of olanzapine. When the entire treatment is considered, this difference has a huge impact on total treatment cost. Similar analysis done by Badarudin et al and Mohammed and Thota, have shown the cost with aprepitant was 36 and 50 times higher than olanzapine-based regimens, respectively.[23,24]

This study contributes to the expanding body of evidence endorsing olanzapine as an effective, well-tolerated, and cost-effective option for the prophylaxis of CINV. Unlike many previous studies, our trial also reports TC as a key outcome, a metric that more closely reflects patient-centered goals.

However, the study has some limitations. Being a single-center, open-label trial, it carries a risk of bias, even though objective outcome measures were used. Anticipatory nausea and vomiting were not assessed. Additionally, subgroup analyses, particularly in patients receiving cisplatin and dacarbazine, were limited by small sample sizes, preventing robust statistical comparisons. Future multicenter studies with larger cohorts and blinding are warranted to confirm these findings and further define the role of olanzapine in different clinical scenarios.

Conclusion

Olanzapine-based OPD regimen offers an effective and cost-efficient alternative to APD regimen for managing CINV in patients receiving HEC. Our findings indicate that OPD not only achieves comparable efficacy in CR and TC rates but also excels in controlling delayed nausea, significantly enhancing QOL of the patients. Given the high incidence of CINV and its impact on patient well-being, olanzapine-based regimens should be considered as first-line treatment option in antiemetic regimens.

Note

This work was presented virtually at the MASCC/ISOO 2021 Conference on June 24, 2021.

Authors' Contributions

We assure that the manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Patients' Consent

Informed consent has been taken from all the patients randomized in this study.

Conflict of Interest

None declared.

Acknowledgments

The authors express their gratitude to the patients, their families, and the staff who participated in their care.

References

1 Sharma R, Tobin P, Clarke SJ. Management of chemotherapy-induced nausea, vomiting, oral mucositis, and diarrhoea. Lancet Oncol 2005;6(02):93–102
2 Hickok JT, Roscoe JA, Morrow GR, et al. Use of 5-HT3 receptor antagonists to prevent nausea and emesis caused by chemotherapy for patients with breast carcinoma in community practice settings. Cancer 1999;86(01):64–71
3 Holdsworth MT, Raisch DW, Frost J. Acute and delayed nausea and emesis control in pediatric oncology patients. Cancer 2006;106 (04):931–940
4 Hesketh PJ, Grunberg SM, Gralla RJ, et al; Aprepitant Protocol 052 Study Group. The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin–the Aprepitant Protocol 052 Study Group. J Clin Oncol 2003;21(22):4112–4119
5 Poli-Bigelli S, Rodrigues-Pereira J, Carides AD, et al; Aprepitant Protocol 054 Study Group. Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting. Results from a randomized, double-blind, placebo-controlled trial in Latin America. Cancer 2003;97(12):3090–3098
6 Schmoll HJ, Aapro MS, Poli-Bigelli S, et al. Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment. Ann Oncol 2006;17(06):1000–1006
7 Navari RM. Profile of netupitant/palonosetron (NEPA) fixed dose combination and its potential in the treatment of chemotherapy-induced nausea and vomiting (CINV). Drug Des Devel Ther 2014;9 (01):155–161
8 Ng TL, Hutton B, Clemons M. Chemotherapy-induced nausea and vomiting: time for more emphasis on nausea? Oncologist 2015; 20(06):576–583
9 Navari RM, Einhorn LH, Passik SD, et al. A phase II trial of olanzapine for the prevention of chemotherapy-induced nausea and vomiting: a Hoosier Oncology Group study. Support Care Cancer 2005;13(07):529–534
10 Passik SD, Navari RM, Jung SH, et al. A phase I trial of olanzapine (Zyprexa) for the prevention of delayed emesis in cancer patients: a Hoosier Oncology Group study. Cancer Invest 2004;22(03):383–388
11 Passik SD, Lundberg J, Kirsh KL, et al. A pilot exploration of the antiemetic activity of olanzapine for the relief of nausea in patients with advanced cancer and pain. J Pain Symptom Manage 2002;23(06):526–532
12 National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Antiemesis [v.2.2024]. 2024
13 GraphPad Prism version 10.0.0 for Windows, GraphPad Software, Boston, Massachusetts, USA. Accessed September 2, 2025 at: www.graphpad.com
14 Kuchuk I, Bouganim N, Beusterien K, et al. Preference weights for chemotherapy side effects from the perspective of women with breast cancer. Breast Cancer Res Treat 2013;142(01):101–107
15 Navari RM, Einhorn LH, Loehrer PJ Sr, et al. A phase II trial of olanzapine, dexamethasone, and palonosetron for the prevention of chemotherapy-induced nausea and vomiting: a Hoosier oncology group study. Support Care Cancer 2007;15(11):1285

16 Navari RM, Gray SE, Kerr AC. Olanzapine versus aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a randomized phase III trial. J Support Oncol 2011;9(05):188–195
17 Tan L, Liu J, Liu X, et al. Clinical research of olanzapine for prevention of chemotherapy-induced nausea and vomiting. J Exp Clin Cancer Res 2009;28(01):131
18 Babu G, Saldanha SC, Kuntegowdanahalli Chinnagiriyappa L, et al. The efficacy, safety, and cost benefit of olanzapine versus aprepitant in highly emetogenic chemotherapy: a pilot study from South India. Chemother Res Pract 2016;2016:3439707
19 Zhang Z, Zhang Y, Chen G, et al. Olanzapine-based triple regimens versus neurokinin-1 receptor antagonist-based triple regimens in preventing chemotherapy-induced nausea and vomiting associated with highly emetogenic chemotherapy: a network meta-analysis. Oncologist 2018;23(05):603–616
20 Sarma I, Buragohain S, Lahon J, et al. Olanzapine versus aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a systematic review and meta-analysis. Cureus 2025;17(04): e83118
21 Shivaprakash G, Udupa KS, Sarayu V, et al. Olanzapine versus aprepitant for the prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving doxorubicin-cyclophosphamide regimen: a prospective, nonrandomized, open-label study. Indian J Pharmacol 2017;49(06):451–457
22 Bloechl-Daum B, Deuson RR, Mavros P, Hansen M, Herrstedt J. Delayed nausea and vomiting continue to reduce patients' quality of life after highly and moderately emetogenic chemotherapy despite antiemetic treatment. J Clin Oncol 2006;24(27): 4472–4478
23 Mohammed O, Thota NK. Efficacy, safety, and cost-effectiveness of reduced-dose olanzapine versus aprepitant as a part of triple-antiemetic therapy in the prevention of chemotherapy-induced nausea and vomiting. J Clin Oncol 2022;40:e24078–e24078
24 Badarudin NS, Mohamed Shah N, Mohd Tahir NA, et al. Health-related quality of life and economic analysis of olanzapine versus aprepitant in preventing chemotherapy-induced nausea and vomiting in patients receiving highly emetogenic chemotherapy in Malaysia. Value Health Reg Issues 2024;44:101028

