Original Research Article

A comparative study of efficacy of olanzapine and aprepitant in prevention of chemotherapy induced nausea and vomiting in a tertiary care hospital

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Abstract

Aims: To compare the efficacy of Olanzapine and Aprepitant in prevention of chemotherapy induced nausea and vomiting and To compare the side effects of both the drugs. To evaluate the cost benefits of both the drugs. **Materials and methods:** A comparative study conducted in All the patients attending outpatient and inpatient department for chemotherapy at MNJ cancer hospital, Osmania Medical College, Hyderabad. It is the largest tertiary care center in the state of Telangana, in 30 patients for a period of 18 months **Results**: In study mean age was 53.47±8.33 years. All the cases among the study patients of both the groups experiences mild vomiting. Among Olanzapine group, one case had severe nausea. Among Olanzapine group, two cases had delayed nausea. The association between the type of the drug with acute vomiting, acute nausea, delayed vomiting a and delayed nausea was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy. The mean price per cycle of olanzapine is 40 INR, when compared to Aprepitant which is 1500 INR. This huge difference between the cost makes Olanzapine the most cost effective drug especially and Low and Middle Income settings. No other drug side effects were noted during the study period.**Conclusion**: Keeping in view the cost of the drug, Olanzapine can be considered in low and middle income settings. Olanzapine is the better, safe, cost effective alternative than Aprepitant.

Keywords: Olanzepine, Aprepitant, Mild vomiting.

Introduction

Chemotherapy-induced nausea and vomiting (CINV) is one of the most common and serious adverse effect. It is associated with a significant deterioration in quality of life and is perceived by patients as a major adverse effect of the treatment[1].In addition patients may be unwilling to continue chemotherapy treatment. Failure to control nausea and vomiting may lead to electrolyte imbalance, malnutrition, delay the discharge from hospital. CINV is a common occurrence after chemotherapy especially with highly emetic chemotherapy (HEC) drugs. Highly emetogenic anticancer drugs were those as defined by Hesketh; Level 4 and Level 5 drugs associated with emesis- producing frequency of 60%–90% and more than 90%, respectively[2].Current prevention strategies include using serotonin receptor, corticosteroids and/or neurokinin 1 receptor antagonists (NK1RA). Many guidelines such as American Society of Clinical Oncology, National Comprehensive Cancer Network(NCCN), and Multinational Association of Supportive Care in Cancer (MASCC), recommend NK1RA-containing regimens for prophylaxis of CINV in patients receiving highly emetogenic chemotherapy (HEC).Although NK1RA-containing regimens significantly improve the control of acute and delayed emesis in patients receiving HEC, these regimens are underused in resource-limited settings because of the unavailability and high cost of NK1RA agents[3]. NCCN guideline version 2.2016 recommended an olanzapine-containing regimen as a less costly alternative for prevention of CINV in patients receiving HEC.

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Aprepitant is a neurokinin-1(NK-1) receptor antagonist. It is given orally with a corticosteroid and a 5-HT3 antagonist, in the prevention of acute and delayed nausea and vomiting associated with HEC. Moreover, the median total cost of APT therapy alone per cycle was found to be 1215 Indian Rupees[4].Olanzepine is an atypical (second-generation) antipsychotic that is a Dopamine (D_{1-4}) and $5HT_2$ receptor antagonist, with a much lower price, can be an effective alternative to NK1RAs.It is an effective agent for the prevention of CINV used in combination with a corticosteroid and $5HT_3$ antagonist. There are very limited studies that compared the efficacy, adverse events and cost-effectiveness of both the regimens. Hence this study was taken up to study the efficacy, adverse events and cost-effectiveness of both the drugs. We aim to compare the efficacy of Olanzapine and Aprepitant in prevention of chemotherapy induced nausea and vomiting.

Materials and methods

A comparative study conducted in all the patients attending outpatient and inpatient department for chemotherapy at MNJ cancer hospital, Osmania Medical College, Hyderabad. It is the largest tertiary care center in the state of Telangana, in 30 patients for a period of 18 months. All the patients, satisfying the inclusion criteria were enrolled into the study. Ethical clearance was obtained from the Institutional Ethical Committee, Osmania Medical College, Hyderabad.

Inclusion Criteria: Age group above 18 years of both gender, Chemotherapy patients receiving highly emitogenic drugs**,** Patients who were on Olanzepine and Aretriptant as antiemetic prophylactic therapy.

Exclusion criteria: Patients of age < 18 years, Patients who are on drugs other than Olanzapine and Aretriptant as antiemetic prophylactic therapy, who are allergic to Olanzapine and Aretriptant, tumors with brain metastasis., who are having cardiopulmonary,

renal abnormalities, Pregnant and lactating mothers, Patients with nausea and vomiting before starting chemotherapy,with motion sickness and Patients who are already on anti emetic drugs even before the starting of chemotherapy.

Procedure

The patients who satisfied the inclusion criteria for chemotherapy at MNJ cancer hospital were enrolled after written informed consent. A detailed medical history, general physical examination was done and findings were recorded at the time of screening.

Patients were assigned into two groups:

Group Olanzapine:

Day 1: Tablet Olanzapine 10 mg per oral 30 minutes before chemotherapy.

Day 2-4: Tablet Olanzapine 10 mg per oral once daily.

Group Aprepitant:

Day 1: Capsule Aprepitant 125 mg per oral 30 minutes before chemotherapy.

Day 2-4: Capsule Aprepitant 80 mg per oral once daily.

Study Outcome: Study outcomes of nausea and vomitingare compared using Multinational Association of **Supportive Cam in Cancer (MASCC) antiemetic tooland Common Terminology Criteria for Adverse Events (CTCAE) tool.**

Complete response (CR) which is defined as number of patients who have achieved no nausea and no vomiting.

The severity of nausea and vomiting was assessed by the IVIAT and Common Terminology Criteria for Adverse Events (CTCAE) version 5, respectively.

Severity scores of nausea are graded as

- Mild: score 1-4
- Moderate: score 5-7
- Severe: score 8-10

Severity scores of Vomiting are graded according to CTCAE grading:

- Grade I: Intervention not required.
- Grade II: Outpatient IV hydration needed. Intervention required.
- Grade III: Tube feeding/TPN needed. Requires Hospitalization
- Mild – Moderate is Grade I and II
- Severe is grade III.

Data Entry and Analysis

The data was entered in Microsoft Excel 2010 version. Data was analyzed using Microsoft Excel 2010 and Epi Info 7.2.0. Descriptive and inferential statistical analysis were used in the present study. Results on continuous measurements were presented on Mean±SD (Min-Max) and results on categorical measurements were presented in Number (%). Significance was assessed at 5% level of significance. Student t-test was used to compare inter group variation for continuous variables. Chi square test was used to compare categorical variables.

Results

Table 1: showing the age distribution of study population

Age group	Olanzapine	Frequency (%)	Aprepitant	Frequency(%)
<40 years	1	8.33	2	11.11
41-45 years	3	25	4	22.22
46-50 years	2	16.66	3	16.66
51-55 years	3	25	4	22.22
56-60 years	2	16.66	3	16.66
>60 years	1	8.33	2	11.11
Total	12	100	18	100
Mean±Standard Deviation	51.43±7.52 years		53.47±8.33 years	
Gender				
Male	5	41.66	5	27.77
Female	7	58.33	13	72.22
Comorbidities				
Yes	5	41.66	6	33.33
No	7	58.33	12	66.66
Type of Co-morbidities				
Diabetes	1	8.33	2	11.11
Hypertension	1	8.33	2	11.11
Both	3	25	2	11.11
None	7	58.33	12	66.66
Total	12	100	18	100

Among Olanzapine group majority (25%) of the patients belonged to the age group of 41-45 years and 51-55 years each, followed by 46-50 years and 56-60 years each (16.66%). 8.33% belonged to the age group of <40 years and >60 years each. The mean age was 51.43±7.52 years.Among Aprepitant group majority (22.22%) of the patients belonged to the age group of 41-45 years and 51-55 years each, followed by 46-50 years and 56-60 years each (16.66%). 11.11% belonged to the age group of <40 years and >60 years each. The mean age was 53.47±8.33 years.Among Olanzapine group, 58.33% were females, 41.66% were males. Among Aprepitant group, 72.22% were females and 27.77% were males. Among Olanzapine group, 41.66% had co-morbidities. Among Aprepitant group, 33.33% had co-morbidities. Among Olanzapine group, 41.66% had co-morbidities, out of which 8.33% contributed to only diabetes and only hypertension. 25% had both. Among Aprepitant group, 33.33% had co-morbidities, out of which 11.11% contributed to only diabetes, only hypertension and both.

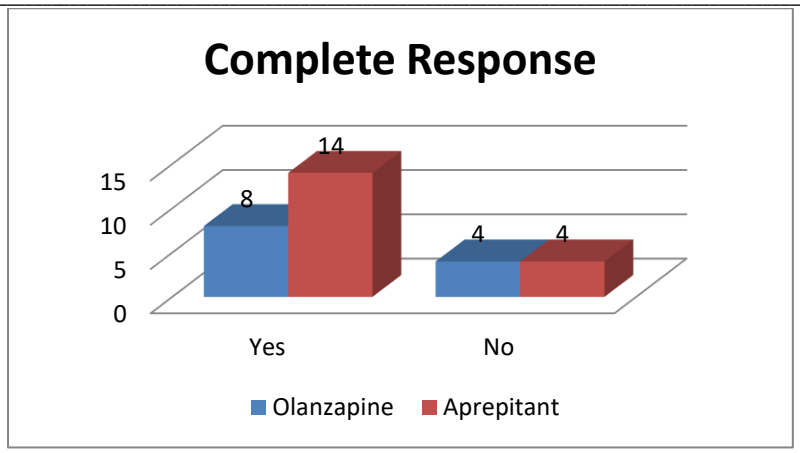

Fig 1: showing the complete response among the groups

Among Olanzapine group, 66.66% had complete response. Among Aprepitant group, 77.77% had complete response.

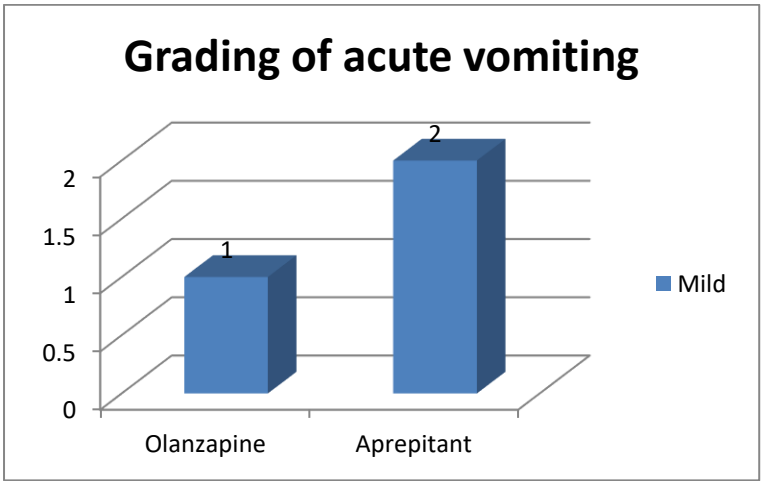

Fig 2: showing the grading of acute vomiting

All the cases among the study patients of both the groups experiences mild vomiting.

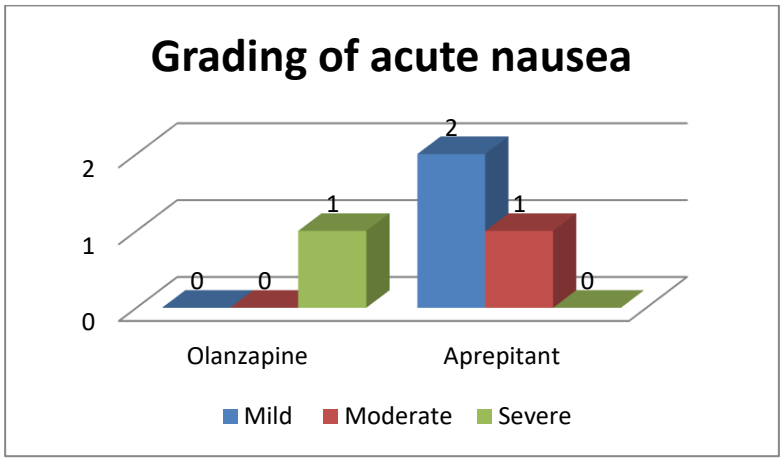

Fig 3: showing grading of acute nausea

Among Olanzapine group, one case had severe nausea. After reporting nausea, one patient discontinued Olanzepine and left the study group. Among Aprepitant group, one cases had mild and one case had moderate acute nausea.

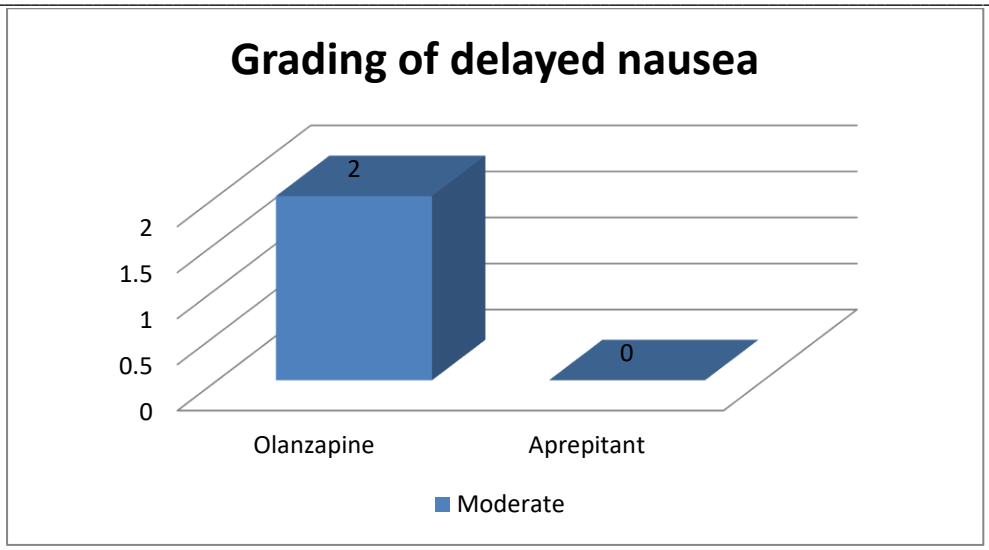

Fig 4: showing grading of delayed nausea

Among Olanzapine group, two cases had delayed nausea.

Table 2: showing the side effects with both the drugs.

Acute vomiting	Olanzapine	Frequency (%)	Aprepitant	Frequency(%)	P value
Yes	1	8.33	2	11.11	0.42 (Not Significant)
No	11	91.66	16	88.88	
Total	12	100	18	100	
Acute nausea					
Yes	1	8.33	3	16.66	0.29 (Not Significant)
No	11	91.66	15	83.33	
Total	12	100	18	100	
Delayed vomitings					
Yes	0	0	0	0	Undefined (Not Significant)
No	11	100	18	100	
Total	11	100	18	100	
Delayed nausea					
Yes	2	18.18	0	0	0.06 (Not Significant)
No	9	81.81	18	100	
Total	11	100	18	100	

The association between the type of the drug and acute vomiting was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced acute vomiting. The association between the type of the drug and acute nausea was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced acute nausea.The association between the type of the drug and delayed vomiting cannot be defined statistically. It means that both the drugs are comparable in terms of chemotherapy induced delayed vomiting.The association between the type of the drug and delayed nausea was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced delayed nausea.The mean price per cycle of olanzepine is 40 INR, when compared to Aprepitant which is 1500 INR. This huge difference between the cost makes Olanzepine the most cost effective drug especially and Low and Middle Income settings. No other drug side effects were noted during the study period.

Discussion

In the present study, among Olanzapine group majority (25%) of the patients belonged to the age group of 41-45 years and 51-55 years each, followed by 46-50 years and 56-60 years each (16.66%). 8.33% belonged to the age group of <40 years and >60 years each. The mean age was 51.43±7.52 years. Among Aprepitant group majority (22.22%) of the patients belonged to the age group of 41-45 years and 51-55 years each, followed by 46-50 years and 56-60 years each (16.66%). 11.11% belonged to the age group of <40 years and >60 years each. The mean age was 53.47±8.33 years.

Table 3:The findings of the present study can be compared with the following studies

Author	Findings	
	Olanzapine group	Aprepitant group
Age		
Present study	The mean age was 51.43±7.52 years.	The mean age was 53.47±8.33 years.
Shivaprakash G et al[5]	The mean age was 47±9.4 years.	The mean age was 45±12 years.
Babu Get al[6]	The mean age was 43.30 years.	The mean age was 44.78 years.
Mukesh S et al[7]	The median age was 48 years ranging from 29-80 years.	

Gender		
Present study	58.33% were females, 41.66% were males.	72.22% were females and 27.77% were males.
Shivaprakash G et al[5]	All the patients were females (Breast cancer)	
Babu G et al[6]	There was female preponderance among study subjects in both the groups.	
Comorbidities		
Present study	41.66% had co-morbidities, out of which 8.33% contributed to only diabetes and only hypertension. 25% had both.	33.33% had co-morbidities, out of which 11.11% contributed to only diabetes, only hypertension and both.
Shivaprakash G et al[5]	75% had no co-morbidities. 5% had only hypertension, 10% had only diabetes, 5% had both diabetes and hypertension.	73% had no co-morbidities. 4.4% had only hypertension, 1.7% had only diabetes, 5% had both diabetes and hypertension.
Acute vomiting		
Present study	8.33% had acute vomiting	11.11% had acute vomiting
Shivaprakash G et al	15% had acute vomiting	0% had acute vomiting
Nivari et al[8]	3% had acute vomiting	3% had acute vomiting
Mukesh S et al[7]	9% had acute vomiting	9% had acute vomiting
Acute nausea		
Present study	8.33% had acute nausea	16.66% had acute nausea
Shivaprakash G et al	15% had acute nausea	26% had acute nausea
Babu G et al[6]	16% had acute nausea	12% had acute nausea
Nivari et al[8]	13% had acute nausea	13% had acute nausea
Mukesh S et al[7]	16% had acute nausea	31% had acute nausea
Delayed vomiting		
Present study	0% had delayed vomiting	0% had delayed vomiting
Shivaprakash G et al	0% had delayed vomiting	0% had delayed vomiting
Nivari et al[8]	23% had delayed vomiting	27% had delayed vomiting
Mukesh S et al[7]	26% had delayed vomiting	17% had delayed vomiting
Delayed nausea		
Present study	18.18% had delayed nausea	0% had delayed nausea
Shivaprakash G et al	0% had delayed nausea	0% had delayed nausea
Babu G et al[6]	12% had delayed nausea	16% had delayed nausea
Nivari et al[8]	31% had delayed nausea	38% had delayed nausea
Mukesh S et al[7]	42% had delayed nausea	45% had delayed nausea

In the present study, among Olanzapine group, 58.33% were females, 41.66% were males. Among Aprepitant group, 72.22% were females and 27.77% were males.In the present study, among Olanzapine group, 41.66% had co-morbidities, out of which 8.33% contributed to only diabetes and only hypertension. 25% had both. Among Aprepitant group, 33.33% had co-morbidities, out of which 11.11% contributed to only diabetes, only hypertension and both.In the present study, among Olanzapine group, 8.33% had acute vomitings. Among Aprepitant group, 11.11% had acute vomitings.In the present study, among Olanzapine group, 8.33% had acute nausea. After reporting nausea, one patient discontinued Olanzepine and left the study group. Among Aprepitant group, 16.66% had acute nausea. In the present study, among Olanzapine group, none of them had delayed vomiting. Among Aprepitant group, none of them had delayed vomiting.In the present study, among Olanzapine group, 18.18% had delayed nausea. Among Aprepitant group, none of them had delayed nausea.In the present study, among Olanzapine group, 66.66% had complete response. Among Aprepitant group, 77.77% had complete response.

Table 4: The findings of the present study can be compared with the following studies

Author	Findings	
	Olanzapine group	Aprepitant group
Present study	66.66% had overall complete response	77.77% had overall complete response
Shivaprakash G et al[5]	85% had overall complete response	81% had overall complete response
Babu G et al[6]	80% had overall complete response	78% had overall complete response
Mukesh S et al[7]	70% had overall complete response	83% had overall complete response

In the present study, among all the cases among the study patients of both the groups experiences mild vomiting. Among Olanzapine group, one case had severe acute nausea.After reporting nausea, one patient discontinued Olanzepine and left the study group.In the present study, among Aprepitant group, one cases had mild and one case had moderate delayed nausea.Among Olanzapine group, two cases had delayed moderate nausea.In the present study, the association between the type of the drug and acute vomiting was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced acute vomiting.In the present study, the association between the type of the drug and acute nausea was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced acute nausea.In the present study, the association between the type of the drug and delayed vomiting cannot be defined statistically. It means that both the drugs are comparable in terms of chemotherapy induced delayed vomiting.

In the present study, the association between the type of the drug and delayed nausea was not statistically significant. It means that both the drugs are comparable in terms of chemotherapy induced delayed nausea.In the present study, the mean price per cycle of olanzepine is 40 INR, when compared to Aprepitant which is 1500 INR. This huge difference between the cost makes Olanzepine the most cost effective drug especially and Low and Middle Income settings.

In the present study, No drug side effects were noted during the study period and in correlation with other studies[5-8].

Conclusion

The objective of the present study was to compare the efficacy of Olanzapine and Aprepitant in prevention of chemotherapy induced nausea and vomiting.Though there was no statistically significant association was derived between the drugs regarding superior efficacy, Aprepitant appears to be better than Olanzepine. However, keeping in view the cost of the drug, Olanzepine can be considered in Low and Middle Income settings.Olanzepine is the better, safe, cost effective alternative than Aprepitant.

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