Original Research Article

# A Prospective Comparative Study Of Efficacy of Olanzapine and Aprepitant in Prevention of Chemotherapy Induced Nausea and Vomiting in GMC, Jammu

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**Received: 19-05-2021 / Revised: 08-07-2021 / Accepted: 06-08-2021**

## Abstract

**Introduction:**Breast cancer ranks first among all cancers in women globally as well as in India, with an incidence rate of 25.8 per 100,000.The combination of anthracyclines with cyclophosphamide forms the basis of many breast cancer treatment protocols. This combination is known to have a high potential for chemotherapy-induced nausea and vomiting (CINV).**Materials and Methods:**A comparative study conducted in all the patients attending outpatient and inpatient department for chemotherapy at Department of Radiotherapy, Govt Medical College, Jammu in 60 patients for a period of 12 months. All the patients, satisfying the inclusion criteria were enrolled into the study. The patients who satisfied the inclusion criteria for Department of Radiotherapy, Govt Medical College, Jammu were enrolled after written informed consent. A detailed medical history, general physical examination was done and findings were recorded at the time of screening. **Results:**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.AmongAprepitant 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.**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.

**Keywords:** Breast cancer, olanzapine, aprepitant, Nausea, vomiting.



## Introduction

Breast cancer ranks first among all cancers in women globally as well as in India, with an incidence rate of 25.8 per 100,000.The combination of anthracyclines with cyclophosphamide forms the basis of many breast cancer treatment protocols. This combination is known to have a high potential for chemotherapy-induced nausea and vomiting (CINV)[1].

Nausea is being rated as the first and vomiting as the third most distressing side effects of cancer chemotherapy[2].With the introduction of neurokinin 1 receptor antagonist (NK1RA) as an antiemetic prophylaxis, additional improvement in CINV control was observed, and as a testimony, it was considered as an essential drug in the prophylaxis regimen in all the major international guidelines such as American Society of Clinical Oncology, National Comprehensive Cancer Network, and Multinational Association of Supportive Care in Cancer (MASCC)[3]

However, breakthrough CINV persists to the extent of 30%–40% in patients even with guideline-directed prophylactic antiemetics.This is more troublesome in breast cancer patients on chemotherapy as only 33% of the patients achieve the complete absence of nausea despite using aprepitant (APT)[4]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[5]. Olanzepine is an atypical (second-generation) antipsychotic that is a Dopamine (D1-4) and 5HT2 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 5HT3 antagonist[6,7].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 tocompare 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 Department of Radiotherapy, Govt Medical College, Jammu in 60 patients for a period of 12 months. All the patients, satisfying the inclusion criteria were enrolled into the study.

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**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 Department of Radiotherapy, Govt Medical College, Jammu 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 severityof 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**

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.AmongAprepitant 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.

**Table 1: Age Distribution**

| S.No | Age Group | Olanzapine | Number (%) | Aprepitant | Number (%) |
|---|---|---|---|---|---|
| 1 | <40 years | 2 | 8.33 | 4 | 11.11 |
| 2 | 41-45 years | 6 | 25 | 8 | 22.22 |
| 3 | 46-50 years | 4 | 16.66 | 6 | 16.66 |
| 4 | 51-55 years | 6 | 25 | 8 | 22.22 |
| 5 | 56-60 years | 4 | 16.66 | 6 | 16.66 |
| 6 | >60 years | 2 | 8.3 | 4 | 11.11 |
| 7 | Total | 24 | 100 | 36 | 100 |

**Table 2: Gender Distribution**

| S.No | Gender | Olanzapine | Number (%) | Aprepitant | Number (%) |
|---|---|---|---|---|---|
| 1 | Male | 10 | 41.66 | 10 | 27.77 |
| 2 | Female | 14 | 58.33 | 26 | 72.22 |

**Table 3: Types of Comorbidities**

| S.No | Gender Types of Comorbidities | Olanzapine | Number (%) | Aprepitant | Number (%) |
|---|---|---|---|---|---|
| 1 | Diabetes | 2 | 8.33 | 4 | 11.11 |
| 2 | Hypertension | 2 | 8.33 | 4 | 11.11 |
| 3 | Both | 6 | 25 | 4 | 11.11 |
| 4 | None | 14 | 58.33 | 24 | 66.66 |
| 5 | Total | 24 | 100 | 36 | 100 |

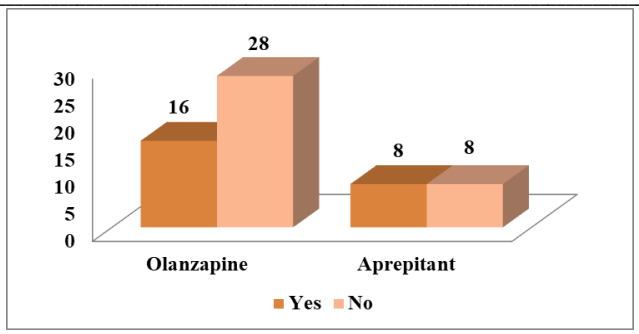


**Fig 1: Complete response among the groups**

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

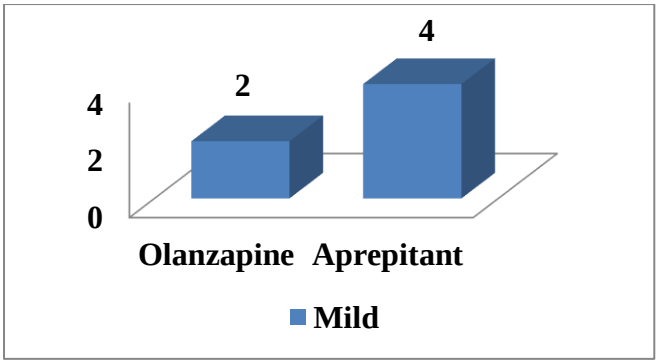


**Fig 2: Grading of acute vomiting among the groups**

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

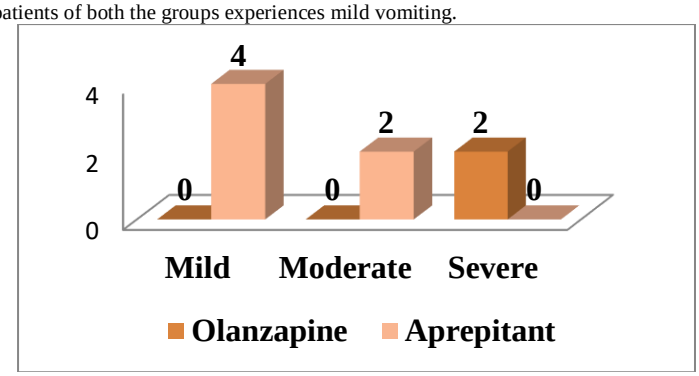


**Fig 3: Grading of acute nausea among the groups**

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.

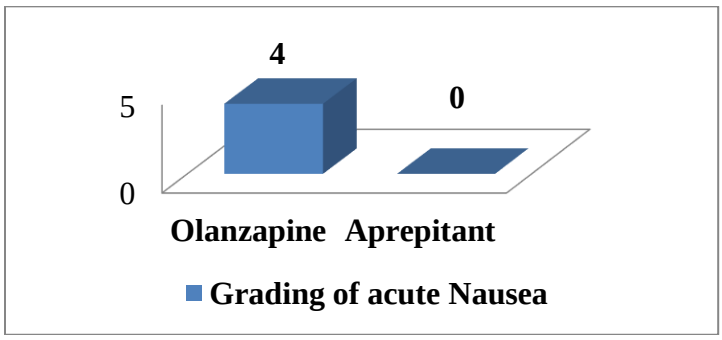


**Fig 4: Grading of delayed nausea among the groups**

**Table 4: Adverse effects**

| Acute vomiting | Olanzapine | Number (%) | Aprepitant | Number (%) |
|---|---|---|---|---|
| Yes | 2 | 8.33 | 4 | 11.11 |
| No | 22 | 91.66 | 32 | 88.88 |
| Total | 24 | 100 | 36 | 100 |
| Acute Nausea | | | | |
| Yes | 2 | 8.33 | 6 | 16.66 |
| No | 22 | 91.66 | 30 | 83.33 |
| Total | 24 | 100 | 36 | 100 |
| Delayed vomiting | | | | |
| Yes | 0 | 0 | 0 | 0 |
| No | 22 | 100 | 36 | 100 |
| Total | 22 | 100 | 36 | 100 |
| Delayed Nausea | | | | |
| Yes | 4 | 18.18 | 0 | 0 |
| No | 18 | 81.81 | 36 | 100 |
| Total | 22 | 100 | 36 | 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.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, 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 vomiting[8]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.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 [9,10] In the present study, among Aprepitant group, one case 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 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.

**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 between the drugs regarding superior efficacy, Aprepitant appears to be better than Olanzepine. However, keeping in view the cost of the drug, Olanzapine can be considered in Low and Middle Income settings. Olanzapine is a better, safe, cost effective alternative than Aprepitant.

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**Conflict of Interest: Nil**

**Source of support:Nil**