Research Article

An Observational Study to Evaluate the Efficacy and Quality of Life Provided by Netupitant and Palonosetron Regimen against Ondansetron in Management and Prevention of CINV

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ABSTRACT

Cancer is a public health concern amongst millions of humans and claims hundreds of lives every year. The maximum worry-inducing side effect of cancer treatment is nausea and vomiting. Therefore, stopping and managing chemotherapy-induced nausea and vomiting is an important part of a cancer patient's treatment plan. In this study, we evaluated the efficacy and quality of life provided by two commonly used antiemetic regimens in the management and prevention of chemotherapy-induced nausea and vomiting (CINV) in cancer patients. We assessed patient-reported nausea, vomiting, use of rescue medication, and Functional Living Index-Emesis (FLIE) questionnaire results, and used them as parameters to make comparisons. We also examined the percentage of patients showing complete response (CR; no emesis and non-use of rescue antiemetics), and the impact of CINV on patient's daily life during the acute and delayed phases. The results show that the complete response is achieved by 26 patients in group-B and 18 patients in group-A, from the total 60 patients, while the FLIE scores indicated better quality of life is maintained in group-B (76.6%). In the study, the predominance of Netupitant and Palonosetron regimen to Ondansetron was demonstrated.

Keywords: Netupitant; Palonosetron; Ondansetron; Chemotherapy induced nausea and vomiting.

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INTRODUCTION

Cancer is a collection of diseases related to peculiar cell growth with the capability to invade or unfold to other parts of the body. The common modality used to treat cancer is Chemotherapy, and it has its toxicity and side effects even though it improves survival in cancer patients. The major non-hematologic toxicity associated with chemotherapy is nausea and vomiting. They not only affect the quality of life of the patient but also his compliance with the treatment. To avoid the clinical sequelae of CINV like malnutrition, dehydration, dyselectrolytemias, anorexia, stress, esophageal tears, and anxiety it is imperative to provide prophylaxis and treatment to CINV.

One such treatment is the Akynzeo regimen, which is a combination of Palonosetron, a serotonin-3 (5-HT3) receptor antagonist, and Netupitant, a substance P/neurokinin-1 (NK-1) receptor antagonist. Palonosetron prevents nausea and vomiting during the acute phase, whereas Netupitant prevents nausea and vomiting during both the acute and delayed phases of chemotherapy. It is given with Dexamethasone in adults to prevent acute and delayed nausea and vomiting associated with initial and repeated courses of cancer chemotherapy including but is not limited to highly emetogenic chemotherapy (HEC). It is available as a hard gelatine capsule (300mg Netupitant, 0.5mg Palonosetron) with a white body and caramel cap with 'HE1' printed on it. Its adverse reactions include >3% - Headache, asthenia, dyspepsia, fatigue, constipation, and erythema. Similar side effects can be observed with its overdose also.

Another such treatment is through Ondansetron. It is the most commonly used management for CINV. It is indicated for the prevention of nausea and vomiting associated with highly emetogenic cancer, and with initial and repeat courses of moderately emetogenic cancer. It is also used in the patients receiving total body radiation, single high dose or daily fractions to the abdomen, and in postoperative nausea and vomiting. It is available in many forms but Tablet (4mg, 8 mg) form is commonly prescribed. Its adverse Reactions include >5% - headache, malaise, constipation, diarrhea, hypoxia, and fatigue. If overdosed, it can lead to sudden blindness, severe constipation, and hypotension.

MATERIALS AND METHODS

It is a prospective observational study, consisting of two treatment arms, group-A (Ondansetron) and group-B (Akynzeo) with 30 patients each (**Table 1**). It was conducted for 6 months. The patients diagnosed with cancer satisfying Inclusion criteria were enrolled in the study. The inclusion criteria are - Patients scheduled to receive high or moderately emetogenic chemotherapy (HEC/MEC) and antiemetic prevention with Akynzeo® or Ondansetron as deemed medically necessary by the

participating physician independently from this study; At least age ≥ 18 years; Women of childbearing potential consenting to use effective contraception during therapy and up to one month after treatment with Akynzeo.

Table 1: Baseline characteristics

Demographic	Group-A (n=30)	Group-B (n=30)
Age(yr)	53 ± 10.6	50 ± 9.4
Gender, n (%)		
Male	19 (63.3)	19 (63.3)
Female	11 (36.6)	11 (36.6)
HEC, n (%)	18 (60)	18 (60)
MEC, n (%)	12 (40)	12 (40)

Value of age is mean ± SD. No statistically significant differences between the groups (P > 0.05); Independent t-test; group-A (Ondansetron); group-B (Akynzeo)

The patients diagnosed with cancer satisfying Exclusion criteria were not enrolled in the study. The Exclusion Criteria are - Women of childbearing potential who are pregnant, planning on becoming pregnant, or breastfeeding; Patients with hypersensitivity to constitutes of the drug-like active substances, excipients (sorbitol, sucrose, and traces of lecithin), or other ingredients of Akynzeo®; Patients in concomitant use of Pimozide, Terfenadine, Astemizole, or Cisapride; Patients currently enrolled in another clinical trial where antiemetic treatment is pre-specified by the study protocol.

Each patient enrolled in the study received either Akynzeo 300mg or Ondansetron 8mg before as a part of the pre-chemotherapy protocol followed by recommended post-chemotherapy protocol. Patients are monitored for five days following chemotherapy. The responses of two chemotherapy cycles were studied. The complete response rate (no emesis and no rescue medication) was recorded using the NCI-CTCAE (version 5.0) scale which is a set of criteria that are used for categorizing occurred nausea and vomiting into different grades based on the response levels.

The Quality of life (QOL) of the patient is assessed by the FLIE questionnaire. It is a patient-completed multidimensional questionnaire. It is a validated 18-item visual analog scale that captures the information about the effect of CINV on the daily lives of patients and has separate domains for the impact of nausea and vomiting. Each item is scored from 1 (not at all) to 7 (a great deal). The cut-offs for no impact of CINV on QOL is a score of ≤ 18 points, and the moderate impact is a score of < 50 from the maximum possible 126 points. The complete response rates and FLIE questionnaire results of both the treatment groups were compared using an independent sample t-test. All statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 27.0.

RESULTS AND DISCUSSION

The complete response (**Table 3**) was shown by 44 patients (no emesis and no rescue medication) from 60 patients, in whom 18 patients were in group-A (Ondansetron) and 26 patients in group-B (Akynzeo). In the two chemotherapy cycles, an average of thirteen (43.3%) patients had experienced both vomiting and nausea in group-A while five (16.6%) patients experienced it in group-B (**Table 2**). The average number of patients experiencing vomiting episodes in both cycles after administration of Ondansetron is (11.5 ± 1.1) while it was only (4.5 ± 0.86) on Akynzeo, and the difference is statistically significant (P = 0.01). The average number of patients experiencing nausea episodes in both cycles after administration of Ondansetron is (12.5 ± 1.11) while it was (6 ± 1.22) on Akynzeo, and this difference is also statistically significant (P = 0.01).

In both the cycles, the average FLIE score of group-A was (45.8 ± 16.17) and in group-B was (28.6 ± 10.73), and the difference is statistically significant (P =0.012). A total FLIE score (**Figure 1**) greater than 50 (Moderate Loss in QOL) was obtained in 12 patients, of which 11 patients were in group-A and 1 patient was from group-B. A total FLIE score greater than 20 (Mild Loss in QOL) was obtained from only 6 patients in group-B (20%) whereas 15 patients from group-A (50%) showing the significant performance (P = 0.01) of group-B. Further, a total of 12 patients have used rescue medication of which 10 patients are from group-A.

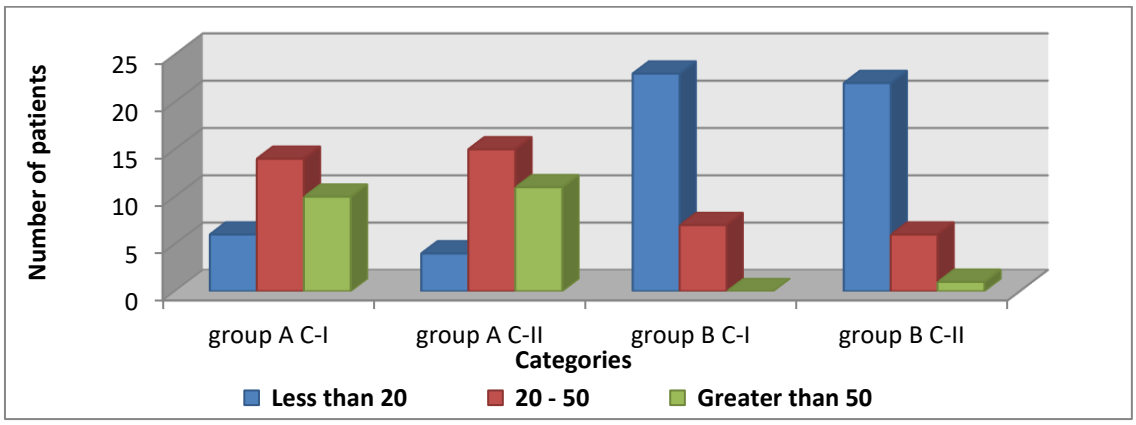

Figure 1: Total Scores in FLIE Scale

Table 2: Incidence of Nausea and Vomiting and Need for Rescue antiemetics

		group-A (n=30)	group-B (n=30)	P value
Cycle - I	**0 – 24 h**			
	Nausea	14 (46.6)	8 (26.6)	0.019
	Vomiting	13 (43.3)	5 (16.6)	0.026
	Rescue antiemetics	7 (23.3)	1 (3.3)	0.045
	24 - 72 h			
	Nausea	13 (43.3)	6 (20.0)	0.039
	Vomiting	11 (36.6)	5 (16.6)	0.038
	Rescue antiemetics	6 (20.0)	4 (13.3)	0.256
Cycle - II	**0 – 24 h**			
	Nausea	12 (40.0)	5 (16.6)	0.037
	Vomiting	11 (36.6)	5 (16.6)	0.034
	Rescue antiemetics	5 (16.6)	2 (6.6)	0.371
	24 - 72 h			
	Nausea	10 (33.3)	5 (16.6)	0.052
	Vomiting	12 (40.0)	3 (10.0)	0.025
	Rescue antiemetics	6 (20)	3 (10.0)	0.320

Values are number of patients (%). group-B ($P < 0.05$) show statistically significant difference with group-A; Fishers exact test; group-A (Ondansetron); group-B (Akynzeo)

Table 3: Complete Response Rate

Phase after chemotherapy	Group-A	Group-B	P-value
	Ondansetron 8mg, % (n = 30)	Netupitant 300mg + Palonosetron 0.5 mg, % (n = 30)	
Acute phase	59	80.83	0.01
Delayed phase	60.8	84.16	
Overall	60	82.5	

CONCLUSION

Chemotherapy-induced nausea and vomiting (CINV) is a major clinical challenge of chemotherapy. It not only hinders the daily performance of the patients but also affects their treatment adherence. The main aim of our study was to evaluate the efficacy and quality of life provided by the Netupitant and Palonosetron regimen against Ondansetron and to understand which provides a better response in the management and prevention of CINV in cancer patients. In this study, the two treatment arms are compared against each other where we found promising results in group-B (Akynzeo). The complete response rate observed in patients of group-B (Akynzeo) predominated over the responses shown by patients in group-A (Ondansetron). Further, this was also supported by FLIE results which indicated that better quality of life is provided by Akynzeo over Ondansetron. All the results calculated were statistically significant. Hence, we conclude that Netupitant and Palonosetron regimen is better in the management and prevention of CINV compared to Ondansetron.

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