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AN OBSERVATIONAL STUDY TO EVALUATE THE SAFETY, EFFICACY, AND QUALITY OF LIFE OF NEPA IN COMPARISON WITH ONDANSETRON IN MANAGEMENT OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING

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ABSTRACT
Cancer is on the public health concerns among millions of people around the world and claims thousands of lives every year. The most fear-inducing side effects of chemotherapy are nausea and vomiting (CINV) which without appropriate antiemetic treatment may lead to experiencing these symptoms in 70%-80% of the cancer patients. Therefore, preventing and managing chemotherapy-induced nausea and vomiting is an important part of care planning for cancer patients. A prospective observational study was carried out to evaluate the safety, quality of life, and effectiveness of NEPA with Ondansetron in managing the patients with chemotherapy-induced nausea and vomiting. The FLIE questionnaire was provided to collect the responses from the patients and the data was given a scoring along with the CTCAE scale. The FLIE response shows that many patients didn't experience nausea nor vomiting. The sample consists of 60 patients including both males and females age 18 years and above. Data was collected for a period of 6 months (September 2020- February 2021) from AOI Hospital, Lingampally and AIG Hospital, Gachibowli, Hyderabad. The results were documented and the data were analysed using SPSS software. Akynzeo showed better quality of life in patients compared to Ondansetron.

KEYWORDS: CINV, NEPA, Ondansetron, FLIE (FUNCTIONAL LIVING INDEX EMESIS), CTCAE**,** SPSS software**.**

INTRODUCTION
Cancer is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. These begin with benign tumours, which do not spread to other parts of the body. Other terms are malignant tumours and neoplasms. One defining feature of cancer is the rapid formation of abnormal cells that grow beyond their usual boundaries and which can then invade adjoining parts of the body and spread to other organs. This process is referred to as Metastasis. Metastases are one of the major causes of death from cancer.

Flie [Functional living index emesis]
FLIE is developed to evaluate the relationship between emesis and patients' daily life activities and is more important to detect the effectiveness of antiemetic treatment compared with other-self diary reports.

Ctcae classification of cinv
Common Terminology Criteria for Adverse Events (CTCAE) are a set of criteria that are used for categorizing the classification of adverse events which is seen in chemotherapy-induced nausea and vomiting**.** It is a system product of the United States National Cancer Institute (US NCI). This scale is used to categorize the occurred nausea and vomiting into different grades based on the response levels.

Nausea grade scaling

Grades	Response
Grade 0	None
Grade 1	Loss Of Appetite Without Alteration In Eating Habits
Grade 2	Oral Intake Decreased Without Significant Weight Loss, Dehydration, Or Malnutrition

Grade3	Inadequate Oral Caloric Or Fluid Intake: Tube Feeding, TPN, Or Hospitalization Indicated.

Vomiting grade scaling

Grade	Response
Grade 0	None
Grade 1	1 To 2 Episodes In 24 Hrs
Grade 2	3 To 5 Episodes In 24 Hrs
Grade 3	>/= 6 Episodes In 24 Hrs: Tube Feeding, TPN, Or Hospitalization Indicated.
Grade 4	Life-Threatening Consequences, Urgent Investigation Indicated
Grade 5	Death

Based on the CTCAE scales of nausea and vomiting, the response level of NEPA is estimated along with the concurrent use of FLIE [functional living index emesis] which helps to assess NEPA effect on the quality of life of the patient**.**

OBJECTIVES

To study the safety, quality of life, and effectiveness of NEPA in comparison with Ondansetron in the management of CINV.

METHODOLOGY

This is a single-arm prospective observational multi-centric study in the department of oncology in the Sunshine Hospitals, Secunderabad, Telangana. This study is designed to evaluate the safety, QOL, and effectiveness of NEPA in comparison with Ondansetron in the management of CINV.

Study Period: The time taken to gather and analyze the data was 6 months i.e. from September 2020 to February 2021.

Study population: 60 patients were included in the study.

Inclusion criteria:

- Patient scheduled to receive high or moderately emetogenic chemotherapy (HEC/MEC).
- Patient scheduled to receive antiemetic prevention with Akynzeo® or Ondansetron as deemed medically necessary by the participating physician independently from this study.
- Age ≥ 18 years.
- Women of childbearing potential must use effective contraception during therapy and up to one month after treatment with Akynzeo.

Exclusion criteria

- Women of childbearing potential those are pregnant, planning on becoming pregnant or breastfeeding.
- Hypersensitivity to active substances, excipients (Sorbitol, sucrose, and traces of lecithin) or other ingredients of Akynzeo®.
- Concomitant use of pimozide, terfenadine, astemizole, or cisapride.
- The patient currently enrolled in another clinical trial where antiemetic treatment is pre-specified by the study protocol.

RESULTS

1. Age of respondents.

Age level	Number of patients
18-30	10
30-50	16
50-70	27
70-80	7

2. Gender of respondents.

Gender	Number of patients
Male	38
Female	22

3. Type of cancers involved in the study population:

Cancers	Regimen	Number of patients with the cancer
Ewing sarcoma	VAC/IE	1
Primary CNS lymphoma	RMPV	1
Breast cancer	CMF	8
Esophageal cancer	DOCE+CARBO	4

Head and neck cancer	DCF	2
Stomach cancer	TPF	6
Cholangiocarcinoma	CAPOX+BEV	1
Soft tissue sarcoma	IFOS ADRIA	3
Endometrial cancer	TAXOL+CARBO	1
Osteosarcoma	CIS+ADRIA or MAP	10
Colorectal cancer	CAPOX	3
Lung cancer	CIS+VIN	7
Gallbladder cancer	XELIIRI	3
Hodgkin's lymphoma	ABVD	1
Prostate cancer	ABIRA+DOCE	1
Krukenberg Tumor	CAPOX	1
Upper cervical Esophageal cancer	TAXOL+CARBO	1
Acute Leukaemia	NHL-BFM-95	1
SCLC	CIS+ETOP	2
Pancreatic cancer	FOLFIRINOX	2
GE junction carcinoma	DCF	1

4. Ctcae representation in a study sample of 30 members in each treatment arm

Patients Who Experienced Vomitings after Taking Ondansetron Represented In a Table 4:

Table 4: CTCAE representation of Vomiting's in ondansetron.

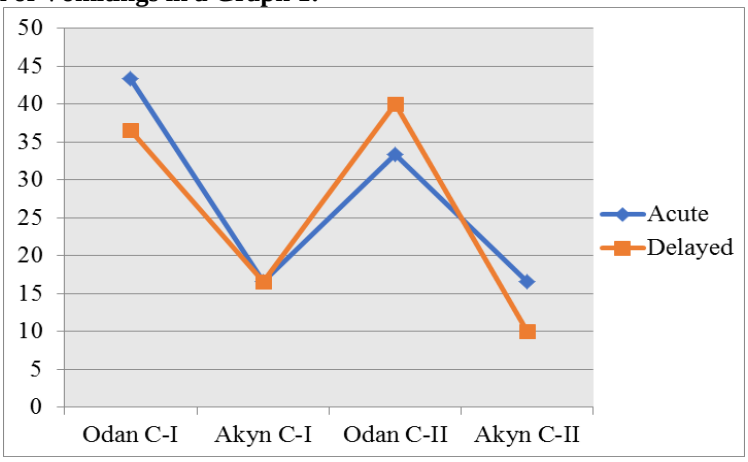
Cycles	Grade 0	Grade 1	Grade 2	Grade 3
CYCLE – I < 24Hrs	17	10	3	0
CYCLE – 1 > 24Hrs	19	9	2	0
CYCLE – II < 24Hrs	20	8	2	0
CYCLE –II > 24Hrs	18	10	2	0

Patients Who Experienced Vomitings after Taking Akynzeo Represented In a Table 5:

Table 5: CTCAE representation of vomitings in akynzeo.

Cycles	Grade 0	Grade 1	Grade 2	Grade 3
CYCLE – I < 24Hrs	25	5	0	0
CYCLE – 1 > 24Hrs	25	4	1	0
CYCLE – II <24Hrs	25	5	0	0
CYCLE –II >24Hrs	27	3	0	0

CTCAE Representation of Vomitings in a Graph 1:



Patients who experienced nausea with ondansetron represented in a Table 6:

Table 6: CTCAE representation of nausea in ondansetron.

Cycles	Grade 0	Grade 1	Grade 2	Grade 3
CYCLE – I < 24Hrs	16	7	5	2
CYCLE – 1 > 24Hrs	17	7	5	1
CYCLE – II < 24Hrs	18	7	4	1
CYCLE –II > 24Hrs	19	5	6	0

Patients who experienced nausea with akynzeo represented in a Table 7:

Table 7: CTCAE representation of nausea in akynzeo.

Cycles	Grade 0	Grade 1	Grade 2	Grade 3
CYCLE – I < 24Hrs	22	6	1	1
CYCLE – 1 > 24Hrs	24	5	1	0
CYCLE – II <24Hrs	25	5	0	0
CYCLE –II >24Hrs	25	3	2	0

CTCAE Representation of Nausea in a Graph 2:

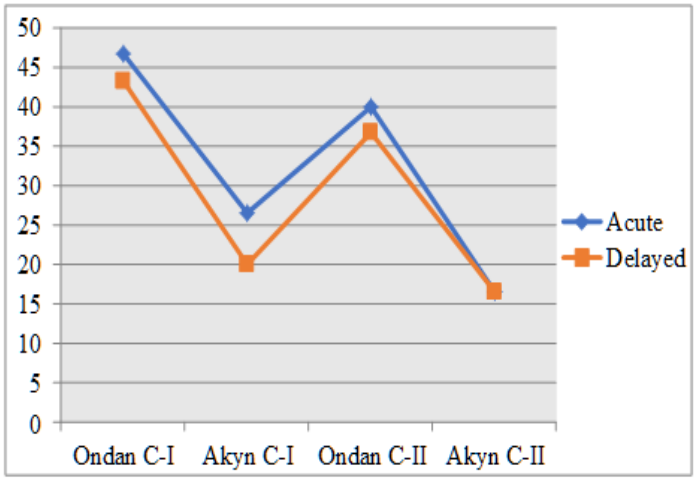


Figure 2: CTCAE representation of nausea.

*C-I denotes to cycle 1 & C-II to cycle 2

Flie outcomes of ondansetron against akynzeo in cycle-i

Flie – Functional living index emesis

Flie Questionnaire has 18 questions with a maximum score of 7 and the least score of 1.

Maximum score – 18* 7 = 126- great deal of pain

Minimum score – 18 * 1 = 18- normal

Table 8: FLIE score contrasting to Quality of Life.

Flie score range	Quality of life
18-45	Normal QOL
45-72	Disturbed QOL
72-99	Bad QOL
99-126	Severely inflicted QOL

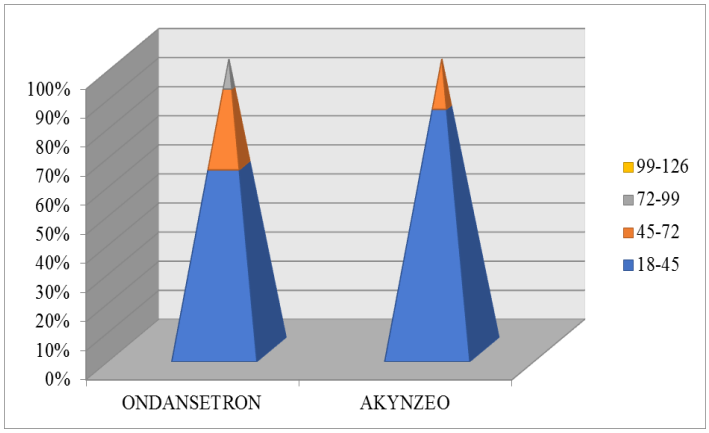


Figure 3: Graphical representation of FLIE scores of the study population in cycle-I.

FLIE questionnaire is collected from each of the 60 member study population. A total of 19 patients experienced the normal quality of life in the Ondansetron group whereas; 25 patients had the normal quality of life in the Akynzeo group. 8 patients had disturbed quality of life in the Ondansetron group whereas; 5 patients had disturbed quality of life in the Akynzeo group. 3 patients had a bad quality of life in the Ondansetron group whereas; none in the Akynzeo group.

Flie outcomes of ondansetron against akynzeo in cycle-ii

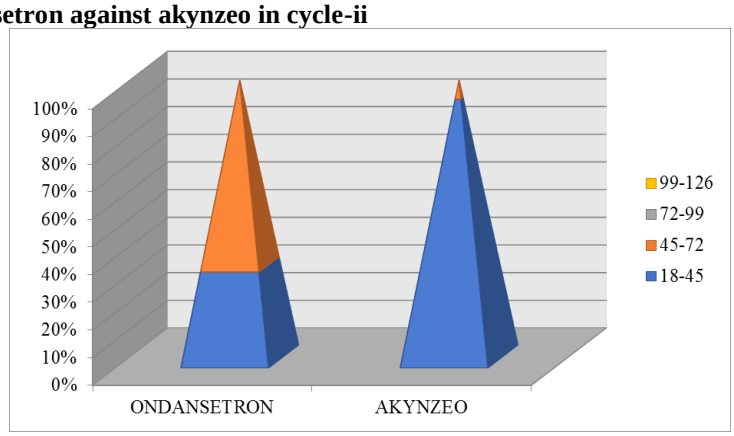


Figure 4: Graphical representation of FLIE scores of the study population in cycle-II.

Cycle-II also followed a similar pattern as such of the cycle-I. The number of people with a normal quality of life is predominantly more in the Akynzeo sample than that of the Ondansetron sample. A total of 10 patients experienced the normal quality of life in the Ondansetron group whereas; 28 patients had the normal quality of life in the Akynzeo group. 20 patients had disturbed quality of life in the Ondansetron group whereas; 2 patients had disturbed quality of life in the Akynzeo group.

Usage outcomes in the study population of 60 members

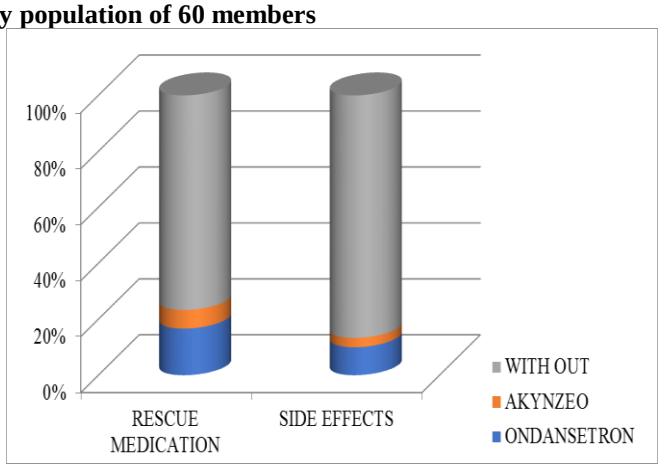


Figure 5: Graphical representation of usage outcomes in the study population.

In this graphical representation, it is clear that the patients who used rescue medications or experienced side effects were found to be more from patients in the Ondansetron group. A total of 10 patients had rescue medication and 6 patients had side effects in the Ondansetron group whereas; only 4 patients had rescue medications and 2 patients experienced side effects in the Akynzeo group. The side effects experienced are ranging from drowsiness, sleepiness, headache, fatigue, and diarrhoea. The rescue medications used are Olanzapine, Promethazine, Dexamethasone, and Octreotide.

Statistical analysis: The study found that Ondansetron control in chemotherapy-induced nausea and vomiting is statistically significantly lower than that of Akynzeo control in chemotherapy-induced nausea and vomitings. Vomiting episodes in cycle-I within 24 hours after administration of Ondansetron (0.55±0.686) are statistically significantly more than that of Akynzeo (0.16±0.374), $t(42)=2.71$, $p=0.01$. This similar pattern was found to be followed for vomitings after 24 hours, nausea episodes with 24 hours and after 24 hours in both cycle-I & II.

The study shows that the quality of life of patients in the Ondansetron group is comparatively lower when contrasted to patients in the Akynzeo group. Q4 of the FLIE questionnaire answered by patients in the Akynzeo group for cycle-I (1.57±0.679) was comparatively better than patients in the Ondansetron group (3.10±1.936), $t(36)=4.09$, $p=0.000$. A similar pattern was observed for all the questions.

The study shows that the quality of life of patients in the Ondansetron group is comparatively lower when contrasted to patients in the Akynzeo group. Q8 of the FLIE questionnaire answered by patients in the Akynzeo group for cycle-I (1.53±0.73) was comparatively better than patients in the Ondansetron group (2.90±1.213), $t(47)=5.28$, $p=0.000$. A similar pattern was observed for all the questions.

DISCUSSION

It is a prospective observational study conducted in 30 patients in each treatment arm. The study duration was 6 months.The majority of respondents are from the age group of 50-70years and male gender.More cases of osteosarcoma, breast cancer, and lung cancer were observed. HEC is found to be at 63.3% in total population while MEC was at 36.6%.A total of 13 (43.3%) and 14 (46.6%) patients had vomitings and nausea in the acute phase of cycle-I respectively in the Ondansetron group whereas; 5 (16.6%), 8(26.6%) patients in Akynzeo group. Eleven (36.6%), 13(43.3%) patients had vomitings and nausea respectively during a delayed phase of cycle-I in the Ondansetron group whereas; 5 (16.6%), 6 (20%) patients in Akynzeo group.A total of 10 (33.3%) and 12 (40%) patients had vomitings and nausea respectively in the acute phase of cycle-II in the Ondansetron group whereas; 5 (16.6%) and 5 (16.6%) patients in Akynzeo group. Twelve (40%) and 11 (36.6%) patients had vomitings and nausea respectively during a delayed phase of cycle-II in the Ondansetron group whereas; 3 (10%) and 5 (16.6%) patients in Akynzeo group.

- FLIE questionnaire is collected from each of the 60 member study population. In cycle-I 8 patients had disturbed quality of life in the Ondansetron group whereas; 5 patients had disturbed quality of life in the Akynzeo group. 3 patients had a bad quality of life in the Ondansetron group whereas; none in the Akynzeo group. In cycle-II 20 patients had disturbed quality of life in the Ondansetron group whereas; 2 patients had disturbed quality of life in the Akynzeo group.A total of 10 patients had rescue medication and 6 patients had side effects in Ondansetron group whereas; only 4 patients had rescue medications and 2 patients experienced side effects in Akynzeo group.The study found that Ondansetron control in chemotherapy-induced nausea and vomiting is statistically significantly lower than that of Akynzeo control in chemotherapy-induced nausea and vomitings. The study shows that the quality of life of patients in the Ondansetron group is comparatively lower when contrasted to patients in the Akynzeo group.

CONCLUSION

Cancer is the leading cause of morbidity and mortality worldwide with thousands of death every year. The main objective of our study was TO EVALUATE THE SAFETY, QUALITY OF LIFE AND EFFECTIVENESS OF NEPA IN COMPARISON WITH ONDANSETRON IN CINV PATIENTS. Various types of cancer patients have been included in our study.

In our study when two treatment arms of both Ondansetron and Akynzeo are compared against each other it is seen that promising results were leaning towards the Akynzeo because of its better control of nausea and vomitings in CINV patients. The results calculated were statistically significant which further proves our belief. Akynzeo showed better quality of life in patients compared to Ondansetron. The overall performance level of Akynzeo is also good when contrasted against Ondansetron. Thereby we conclude that safety, quality of life, and effectiveness of NEPA is better in comparison to Ondansetron in CINV patients.

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