

## Drug Utilization Evaluation of Antiemetics in Chemotherapy Induced Nausea and Vomiting in Oncology Setting

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### Abstract

**Background:** Many of the Patients with carcinoma has poor-quality of life because of their disease conditions. Chemotherapy should improve the quality of life but adverse drug reactions of anticancer drugs are producing nausea and vomiting.

**Objectives:** To assess utilization pattern and appropriateness of antiemetic's in chemotherapy induced nausea and vomiting.

**Methods:** In a prospective study medication orders of patients on chemotherapy for breast cancer were reviewed and patients were interviewed to assess treatment pattern and its appropriateness in Bharath specialty oncology hospital Mysore. Drug selection, dose, route and administration technique used were reviewed with respect to standard international recommendations to evaluate the appropriateness of the antiemetics.

**Results:** 316 patients were followed over six months. In treatments with AC regimen (Doxorubicin + Cyclophosphamide Combination) 48.8% were ondansetron. In PT regimen (Paclitaxel and Carboplatin) treatments 76% with combination of palonosetron, dexamethasone, and Metoclopramide/promethazine. In TC regimen (Docetaxel and Cyclophosphamide) treatments two combinations were dominantly used i.e. Palonosetron with dexamethasone was 29.4% and Ondansetron with dexamethasone was 35.2%. In Paclitaxel alone treatments combination antiemetic Palonosetron with Dexamethasone with/without Promethazine/Metoclopramide were used in 76% treatments. Intriguing part of this dissection is treatments weekly CT cisplatin which is HEC (high emetogenic concentration) and 50.9% were receiving mild antiemetic metoclopramide of which 8 of 26 patients receiving Metoclopramide vomited i.e. 70% of treatments with Metoclopramide in Cisplatin weekly CT were found successful. 93.3% Antiemetic regimens were inappropriate to emetogenic potential of chemotherapy regimen. 45.8% of antiemetic doses in regimen were inappropriate and 27.2% administration errors were found. Here administration error is time gap between premedication antiemetic and chemotherapy which supposed to be at least 30 min and not more than 3.30 hours.

**Conclusion:** The antiemetic used in CINV were not compliant with NCCN guidelines. However most of the treatments which were found non-compliant is justifiable with patients poor economic status or denial of government insurance to fund for Neurokinin 1 antagonist.

**Keywords:** Emetogenic Potential; Cisplatin; Ondansetron; Metoclopramide

### Introduction

Cancer is Deadly disease and it is second leading cause of death worldwide, accounting for 7.6 million deaths (around 13% of all deaths) in 2008. The main types of cancer are lung (1.37 million deaths), stomach (736000 deaths), liver (695000 deaths), colorectal (608000 deaths), breast (458000 deaths) and cervical cancer (275000 deaths). About 30% of cancer deaths are due to the five leading behavioral and dietary risks: high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use and

alcohol use. Tobacco use is the most important risk factor for cancer causing 22% of global cancer deaths and 71% of global lung cancer deaths. Deaths from cancer worldwide are projected to continue rising, with an estimated 13.1 million deaths in 2030 [1].

In India, cancer prevalence is estimated to be around 2.5 million, with over 8,00,000 new cases and 5,50,000 deaths occurring each year due to this disease. Among men, lung, esophagus, stomach, oral and pharyngeal cancers are more prevalent, while in women; cancers of cervix and breast are more prevalent followed

by those of stomach and esophagus [2].

Certainly along with morbidity of disease there are advancements in chemotherapy for treating different type of carcinomas. The advancement in treatment has its benefits in improving patient quality of life and even cure in certain cancers, along with that there are serve Adverse drug reactions like Nausea, vomiting, neutropenia, leucopenia, alopecia, myelosuppression etc. this reactions especially Nausea and vomiting compromise the patients quality life.

Nausea and Vomiting in Chemotherapy and Radiation Therapy patients is very common, so to avoid chemotherapy induced nausea and vomiting there is Prophylaxis treatment with antiemetics is advised to patient as premedication which is administered before chemotherapy. Despite of premedication antiemetic's, patient may have nausea and/or Vomiting which may due to inappropriateness of antiemetic therapy or overwhelmed emetogenicity or patient sensitivity.

Cancer patients rated nausea as their first and vomiting as their third most feared symptoms [3-5]. Inadequately controlled nausea and vomiting can carry significant medical consequences including dehydration and electrolyte imbalance, which would negatively affect patient's quality of life, extend the length of hospitalization and increase the use of health care resources. Such consequences have driven 25 - 50% of patients to refuse continuing or at least delay their chemotherapy regimen [3].

A major concern when treating nausea and vomiting in cancer patients is that health care professionals, mainly nurses and physicians, underestimate the incidence of CINV secondary to chemotherapy with high and moderate emetogenic potential [3].

This was revealed in the results of a survey conducted at Johns Hopkins Cancer Medical Center, Baltimore, which reflected a disparity between health care professionals (physicians and nurses) and patients' perception regarding CINV. In this survey, 83% of physicians and nurses estimated control of acute emesis in patient receiving agents of moderate emetic risk, whereas only 72% overenrolled patients reported that they achieved control of acute emesis [3]. Such discrepancy may partially explain the inadequate compliance rate of health care providers to clinical guidelines. For instance, Kaiser, *et al.* evaluated the adherence to different guidelines.

For anti-emetic treatment provided by the Multinational Association of Supportive Care in Cancer, National Comprehensive Cancer Network (NCCN), the American Society of Health System Pharmacists and the American Society of Clinical Oncology. The results reflected very low adherence of 30 - 50% to existing guidelines. Better implementation of such guidelines was accompanied by better antiemetic outcomes for patients and lower costs [3].

Breakthrough emesis is difficult to control and Poor response to treatment.

Several studies were conducted to determine the rational use of Antiemetic's in management emesis control came out with few findings that are as follows:

1. Study revealed that the majority of the patients were either treated for a shorter duration with corticosteroids or a longer duration with a 5-HT3 antagonist [3].
2. The majority of these patients received chemotherapeutic agents of minimal and low emetogenic potential, where an unindicted combination of a 5-HT3 blocker and a corticosteroid was prescribed [3].
3. 5-HT3 antagonist for more than the recommended duration [3].

In case of inappropriate use of chemotherapy regimens, several studies determined that it may lead to huge drug wastage; thereby drug shortage, unnecessary adverse drug reactions, increased drug resistance and increases unnecessary cost of treatment. Also, there arises a potential mistrust on the real efficacy of Anti-emetic therapy due to its use for inappropriate indications. A drug utilization evaluation study can help us in understanding the prescribing patterns of a drug and possibly the factors influencing the prescribing.

Drug use evaluation is an ongoing, systematic, quality improvement process within a healthcare organization. Implementation of DUE helps to improve the quality and cost-effectiveness of the drug use thereby improving the patient care. In recent years, studies on drug utilization have become a potential tool for the evaluation of health systems. The first and foremost aim of drug utilization evaluation is patient care through optimization of drug therapy. This can be achieved through the ongoing review of use of a drug and other data in a given health care environment. Hence, it was felt essential to systematically review the utilization patterns of anti-emetics used to control the chemotherapy induced nausea and vomiting with respect to standard international recommendations to improve the prescribing pattern and thereby promote rational use of Antiemetics in Prevention and management of chemotherapy induced nausea and vomiting.

## Materials and Methods

The patients who were taking drugs used in present study such as Neurokinin 1 Antagonist, metoclopramide/promethazine, palonosetron, ondansetron, cisplatin were utilized for the present study from bharath cancer hospital, Mysuru. Patient consent form and ethical committee permission was also procured.

**Study Site:** The study was conducted at Bharath Hospital & Institute of Oncology (BHIO). It is a belonging to HealthCare Global (HCG) Enterprises Ltd, the specialist in cancer care. It is a cancer care network with quality care across 27 centres in India. The hospital has various services like medical oncology, surgical oncology, radiation oncology, palliative care and social worker services. Generally, on outpatient basis around 100 patients receive care on daily basis and around 20 new patients will be admitted for diagnosis, follow up and treatment purpose.

**Study Design:** This was a prospective observational study.

**Study Period:** The study was carried out for a period of six months November 1<sup>st</sup> 2013 to April 1<sup>st</sup> 2014.

### Study Criteria

#### Inclusion criteria

- All in patients receiving chemotherapy.
- All patients receiving chemotherapy at day care.
- All patients receiving chemotherapy either with/without radiation.

#### Exclusion criteria

- Patients who were admitted for only Radiation therapy.
- Patients who are non-cooperative or unwilling to sign in formed consent form.

### Results

A total of 328 patients were reviewed and were found to be eligible for study during six months of period. Out of 328 patients reviewed, 316 patients were enrolled in the study and remaining did not agree to participate in the study.

Out of 316 patients, most of them were belonging to age group 50 - 59 years (n = 102, 32.3%) followed by 60-69 years (n = 72, 22.8%) and 40-49 years (n = 56, 17.7%). Majority of the enrolled patients were female (n = 213, 62.4%) and remaining were male (n = 103, 32.6%). On reviewing social habits of the enrolled patients, it was found that majority (n = 236, 75.6%) of the enrolled patients did not have any social habit(s), however, 43 of 316 patients were smokers, 29 of 316 patients were alcoholic and 5 of 316 patients had habit of tobacco chewing. Most of the patients were on mixed diet (n = 166, 52.5%) and remaining were on pure vegetarian diet (n = 150, 47.5%). Looking at the marital status of the patients, most of them were married (n = 288, 91.1%) followed by unmarried (n = 11, 3.55) and widows (n = 10, 3.2%). Detailed demographic and patient related other information are described in table 1.

Patient Characteristics	Number	Percentage (%)
<b>Age (years)</b>		
01 - 19	Nil	Nil
20 - 29	15	4.7
30 - 39	39	12.3
40 - 49	56	17.7
50 - 59	102	32.3
60 - 69	72	22.8
70 - 79	28	8.9
80 - 89	04	1.3
≥ 90	Nil	Nil
<b>Gender</b>		
Male	103	32.6
Female	213	67.4
<b>Social History</b>		
Alcoholic	29	9.2
Smoker	43	13.6
Tobacco chewing	05	1.6
Drug addict	Nil	Nil
None	239	75.6
<b>Diet</b>		
Vegetarian	150	47.5
Mixed Diet	166	52.5
<b>Marital Status</b>		
Married	288	91.1
Unmarried	11	3.5
Separated	7	2.2
Widow	10	3.2

**Table 1:** Demographics and Other Patient Information.

#### Sources of Data

- Patient case records
- Laboratory reports
- Patient or patient's care taker(s) interview
- Treatment chart
- Interviewing healthcare professionals
- Any other relevant source(s)

#### Ethical Approval

Institutional Human Ethical Committee of J.S.S College of Pharmacy, Mysore approved the study.

### Study Procedure

The study involved the following steps:

#### Preparation of data collection form

A specially designed data collection form (Annexure-III) was devised for the study. The particulars included demographic details like name, age, gender, family history, social habits, diet, height, weight, body surface area, address,; clinical data such as diagnosis, past medication history, co-morbidities, allergy status, tumor size, stage of disease therapeutic data such as name of the drug, dose, frequency, route, and duration of administration, concurrent medication(s), laboratory tests and results. The same details were documented electronically in specially designed database using Microsoft Access 2010. To report, document and assess adverse drug reactions due to anti-cancer drugs used for treatment of cancer and Antiemetic used as premedication, standard documentation form of clinical pharmacy department of JSS College of Pharmacy, Mysore.

#### Patient enrollment

Patients fulfilling the study criteria were enrolled into the study after obtaining the informed consent.

Patients were enrolled from in-patients general wards, private wards and day care center.

#### Data collection

All relevant details of the enrolled patients were obtained from various data sources and documented in the data collection form.

#### Assessment of utilization Anti-emetics in the hospital

Utilization evaluation of anti-emetics as premedication and prophylaxis was conducted on qualitative basis. All the enrolled patients were reviewed in terms of chemotherapy regimen prescribed and anti-emetics recommended. Emetogenic potential of Chemotherapy regimen prescribed and anti-emetics used were reviewed with respect to standard international recommendations to evaluate the appropriateness of the anti-emetics used. To evaluate appropriateness of anti-emetics prescribed, National Comprehensive Cancer Network (NCCN) guidelines were used as a standard and to evaluate appropriateness of administration technique, guidelines from Cancer Institute New South Wales, Australia (available at <https://www.eviq.org.au/>) were considered as a standard.

#### Monitoring, evaluation and documentation of adverse drug reactions to anti-emetics

All patients enrolled in the study were monitored for occurrence of adverse reactions to chemotherapeutic agents and anti-emetics. On identification of ADR, all necessary data was collected

and documented in the ADR documentation form. Causality of the ADRs was assessed using the WHO ADR probability scale (Annexure-V) and Naranjo's algorithm (Annexure-VI). The reported ADRs were also assessed for their severity by using the Modified Hartwig and Siegel scale (Annexure-VII). The predictability of the reported reactions was estimated using the predictability scale (Annexure-VIII) and preventability by the Modified Shumock and Thornton criterion (Annexure-IX).

Type of cancer	Number	Percentage (%)
Breast	99	31.4
Head and Neck	70	22.3
Cervical	47	14.9
Lung	30	9.5
Stomach	17	5.4
Ovarian	15	4.7
Colon/rectum	8	2.5
Gynecological	7	2.2
Bladder	5	1.6
Multiple myeloma	5	1.6
Leukemia	3	0.9
Brain	3	0.9
Liver	3	0.9
Non-Hodgkin Lymphoma	3	0.9
Kidney	1	0.3

**Table 2:** Types of cancers observed during study.

During six months of study period breast cancer was most commonly (n = 99, 31.4%) seen followed by head and neck cancers (n = 70, 22.3%), cancer of cervix (n = 47, 14.9%), lung cancer (n = 30, 9.5%). Types of cancer patients reviewed during study are mentioned in table 2.

Recommended Treatment	Number	Percentage (%)
Adjuvant	132	41.7
Neo-adjuvant	57	18.0
Palliative	73	23.1
Primary	54	17.0
Radiation (concomitant with chemotherapy)	146	46.2

**Table 3:** Recommended Treatment for Cancer Patients.

Most of the enrolled patients were receiving treatment as adjuvant chemotherapy (n = 132, 41.7%) followed by palliative chemotherapy (n = 73, 23.1%), neo-adjuvant chemotherapy (n = 57, 18%) and primary chemotherapy (n = 54, 17%). However, 146 of 316 patients were receiving radiation therapy also along with adjuvant or neo-adjuvant chemotherapy.

Emetogenic Potential	Treatment followed at study hospital	No of patient received	No Patients had vomiting	Treatment status	
				Failed	Success
Highly Emetogenic regimens (n = 242)  NCCN Recommendations	5HT3 RA+Steroid+ NK1 Antagonist	14	2	14.2	85.8
	5HT3 RA+Steroid	68	37	54.4	45.6
	5HT3 RA + NK1 Antagonist	6	2	33.3	65.7
	Steroid +NK1 Antagonist	01	1	100	00
	Steroid ± Dopamine antagonists	14	13	92.8	7.2
	5HT3 RA ± Dopamine antagonists	103	60	55.8	44.2
	Dopamine antagonists Only	36	21	58.4	41.6
5HT3 RA+ Steroid+ NK1 Antagonist					

**Table 4:** Prescribing Pattern of Anti-emetic Drugs With High Emetogenic Potential chemotherapeutic regimens.

Emetogenic Potential	Treatment followed at study hospital	No of patient received	No Patients had vomiting	Treatment status	
				Failed	Success
Moderate emetogenic potential (n = 44)  NCCN Recommendations	5HT3 RA+ Steroid + NK1 Antagonist	1	00	00	100
	5HT3 RA+ Steroid	19	2	00	95
	Steroid +NK1 Antagonist	2	00	00	100
	5HT3 RA + NK1 Antagonist	00	00	00	00
	Steroid	4	1	25	75
	5HT3 RA	13	6	46.1	53.9
5HT3 RA+ Steroid ± NK1 Antagonist	Dopamine antagonists (Metoclopramide)	5	3	60	40

**Table 5:** Prescribing pattern of anti-emetic drugs with moderate emetogenic potential.

Emetogenic Potential	Treatment followed at study hospital	No of patient received	No Patients had vomiting	Treatment status	
				Failed	Success
Low to minimal emetogenic potential (n = 30)  NCCN Recommendations	5HT3 RA+Steroid + Dopamine agonist	01	0	0	100
	5HT3 RA+Steroid	14	04	41.6	58.3
	Steroid	2	0	0	100
	5HT3 RA	12	1	8.3	91.6
	Dopamine antagonists (Metoclopramide/ Prochlorperazine)	1	1	100	00
5HT3 RA or Steroid or Dopamine antagonists (Metoclopramide/ Prochlorperazine)					

**Table 6:** Prescribing pattern of anti-emetic drugs for low to minimal emetogenic potential.

High Emetogenic Potential Regimen		
	Appropriate	Inappropriate
Indicated as per emetogenic potential of chemotherapy	(14) 5.8%	(226) 93.3%
Dose	(68) 28.1%	(174) 71.9%
Administration	(66) 27.2%	(176) 72.7%
	49 patients had vomiting	49 patients had vomiting
Moderately Emetogenic Potential Regimen		
	Appropriate	Inappropriate
Indicated as per emetogenic potential of Chemotherapy	(21) 47.7%	(23) 52.3%
Dose	(11) 25%	(33) 75%
Administration	(38) 86.3%	(6) 13.6%
	Only 9 had vomiting	3 patients had vomiting
Low to minimally Emetogenic Potential Regimen		
	Appropriate	Inappropriate
Indicated as per emetogenic potential of Chemotherapy	(15) 50%	(15) 50%
Dose	(8) 26.7%	(14) 73.3%
Administration	(24) 80%	(6) 20%
	Only 2 patients had vomiting	4 patients had vomiting

Table 7: Appropriateness of anti-emetic regimen used for chemotherapy regimens with different emetogenic potential.

Name of the regimen	Drugs used as Pre Medication in No of Patients
AC(43)	Ondansetron (n = 21, 48.8 %) Palonosetron (n = 13, 30.2%) Ondansetron+ Palonosetron (n = 2, 4.6%) Dexamethasone+ Palonosetron (n = 1, 2.3%) Dexamethasone+Ondansetron (n = 2, 4.6%)
AC-Paclitaxel (8)	Dexamethasone+Ondansetron (n = 4, 50 % ) Palonosetron+Dexamethasone+ Ondansetron (n = 1, 12.5%) Palonosetron+Dexamethasone(n = 1, 12.5% ) Aprepitant+ Palonosetron (n = 2, 25%) Aprepitant+ Dexamethasone-1 (12.5%)
Cisplatin (C) (53)	Ondansetron (n = 11, 20.7%) Dexamethasone+Ondansetron (n = 1, 1.8%) Dexamethasone+ Palonosetron (n = 2, 3.7%) Palonosetron (n = 10, 18.8%) Fosaprepitant+ Palonosetron (n = 1, 1.8%) Metoclopramide (n = 27, 50.9%)

Paclitaxel (T) (13)	<p>Palonosetron+Dexamethasone (n = 06, 46.1%)</p> <p>Palonosetron (n = 02, 15.3%)</p> <p>Ondansetron (n = 1, 7.6%)</p> <p>Dexamethasone + Metoclopramide (n = 1, 7.6%)</p> <p>Dexamethasone+Ondansetron (n = 3, 23.0%)</p>
DCF (4)	<p>Ondansetron (n = 2, 50%)</p> <p>Dexamethasone+Ondansetron (n = 1, 25%)</p> <p>Metoclopramide (n = 1, 25%)</p>
PT (46)	<p>Palonosetron+Dexamethasone ± Promethazine/Metoclopramide (n = 35, 76%)</p> <p>Dexamethasone+ Aprepitant (n = 4, 8.6%)</p> <p>Ondansetron (n = 2, 4.3%)</p> <p>Palonosetron (n = 3, 6.5%)</p> <p>Dexamethasone (n = 2, 4.3%)</p>
TC (17)	<p>Ondansetron (n = 2, 11.7%)</p> <p>Palonosetron (n = 2, 11.7%)</p> <p>Palonosetron+Dexamethasone (n = 5, 29.4%)</p> <p>Dexamethasone+ Ondansetron (n = 6, 35.2%)</p> <p>Dexamethasone+ Ondansetron+ Palonosetron (n = 2, 11.7%)</p>
CF (7)	<p>Metoclopramide (n = 3, 42.8%)</p> <p>Palonosetron (n = 3, 42.8%)</p> <p>Ondansetron (n = 1, 14.2%)</p>
FEC (16)	<p>Ondansetron (n = 2, 12.5%)</p> <p>Palonosetron (n = 7, 43.7%)</p> <p>Dexamethasone +Palonosetron/Ondansetron (n = 7, 43.5%)</p>
EC (7)	<p>Palonosetron (n = 2, 28.5%)</p> <p>Dexamethasone +Palonosetron/Ondansetron (n = 2, 28.5%)</p> <p>Ondansetron (n = 3, 42%)</p>
FAC (21)	<p>Dexamethasone (n = 6, 28.5%)</p> <p>Metoclopramide (n = 3, 14.2%)</p> <p>Ondansetron (n = 7, 33.3%)</p> <p>Palonosetron (n = 5, 23.8%)</p>
CMF (4)	<p>Ondansetron (n = 3, 75%)</p> <p>Palonosetron (n = 1, 25%)</p>

**Table 8:** Anti-emetics used with different chemotherapy regimens.

## Discussion

Cancer remains a major health burden in the developing world. Chemotherapy, over the years, have been used in an attempt to reduce the morbidity rates, recurrence rates and increase the survival rates of breast cancer patients. This, however, has resulted in its imprudent use and associated consequences of increased resistance to chemotherapy treatment, unnecessary adverse reactions and inappropriate management of patients. Chemotherapy induced nausea and vomiting (CINV) remains an important adverse effect despite the introduction of new anti-emetic medications as there is less adherence to the guidelines and administration techniques [3].

This work is focussed on assessing the utilization patterns of Antiemetics used in the management or prevention of chemotherapy induced nausea and vomiting at our study site. Risk of nausea and vomiting depends on emetic potential of chemotherapeutic regimen, duration of Antiemetics used, time difference between antiemetic and chemotherapy drug.

A total of 242 patients were screened for highly emetogenic chemotherapeutic agents in a tertiary care hospital, bharath cancer hospital. NCCN recommends using combination of 5HT3 RA, corticosteroids and NK1 antagonists for patients receiving highly emetogenic regimen. 14 of 242 patients received same anti-emetic treatment as recommended as per NCCN guidelines 2014. However, 68 of 242 patients received combination of 5HT3 RA and corticosteroids without NK1 antagonists. Many patients (n = 103) received combination of 5HT3RA and dopamine antagonists and 36 patients received only dopamine antagonists as antiemetic drug for prevention of vomiting due to highly emetogenic drugs.

A total of 44 patients received moderately emetogenic chemotherapeutic agents. NCCN recommends using combination of 5HT3 RA and corticosteroids with or without NK1 antagonists for patients receiving moderately emetogenic regimen. 20 of 44 patients received same anti-emetic treatment as recommended as per NCCN guidelines 2014. However, 13 of 44 patients received only 5HT3RA and 5 of 44 patients received only dopamine antagonists.

A total of 30 patients received low to minimal emetogenic chemotherapeutic agents. NCCN recommends using combination of 5HT3 RA or corticosteroids or dopamine antagonists for patients receiving low to minimal emetogenic regimen. 15 of 30 patients received same anti-emetic treatment as recommended by NCCN guidelines 2014. However, remaining 15 patients received combinations of anti-emetic drugs which are not strongly recommended as per NCCN guidelines 2014.

Appropriateness of anti-emetic prescribing was reviewed with respect to NCCN guidelines and it was found that only 14 of 242 patients received appropriate anti-emetic regimen for prevention of CINV to highly emetogenic drugs. Looking at the dose of anti-emetic only 174 of 242 patients received correct dose of anti-emetic regardless of appropriateness of anti-emetic selected. Administration of selected anti-emetic was appropriate only in 66 patients.

Appropriateness of anti-emetic prescribing was reviewed with respect to NCCN guidelines and it was found that only 21 of 44 patients received appropriate anti-emetic regimen for prevention of CINV to moderately emetogenic drugs. Looking at the dose of anti-emetic only 11 of 44 patients received correct dose of anti-emetic regardless of appropriateness of anti-emetic selected. Administration of selected anti-emetic was appropriate in 38 patients.

Appropriateness of anti-emetic prescribing was reviewed with respect to NCCN guidelines and it was found that only 15 of 30 patients received appropriate anti-emetic regimen for prevention of CINV to moderately emetogenic drugs. Looking at the dose of anti-emetic only 8 of 30 patients received correct dose of anti-emetic regardless of appropriateness of anti-emetic selected. Administration of selected anti-emetic was appropriate in 24 patients.

In our study we found the use old guidelines along the new one made patient treatment costly and over doses. For example we found ondansetron 32 mg is still being prescribed even it is avoided as per new guidelines and palonosetron 0.25 mg is supposed to be administered only on 1<sup>st</sup> day of chemotherapy but in few patient we found the drug has been given for 3 days continuously.

In our observation we found use of dexamethasone 20 mg in many patient which is over dose according to guidelines as according to guidelines it supposed to be 8 - 12 mg and use of promethazine was nowhere recommended in guidelines but in practice we have seen in many patient being administered with this drug along the antiemetic regimen respective to the emetogenic potential of chemotherapy regimen and Metoclopramide is also being used very widely along with or without other antiemetics.

We observed use of NK 1 antagonist was limited because of patient affordability and Government Insurance unwilling to fund for the drug.

In our study we found only 5.7% (14 of 242) of patients receiving highly emetogenic potential Chemotherapy regimen (HEC) received significant therapy. In this 14 patients, only 2 patients vomited. so significant rate was found to be 85%. In remaining 228 patients receiving various antiemetics 134 patients vomited, i.e. in 58.7% treatments failed because of non-adherence to guidelines.

In patients receiving moderately emetogenic potential chemotherapy regimen (MEC) 20 out of 44 treatments i.e. 45.4% was appropriate. In this 20 patients only 2 patients i.e. 1% had vomiting. In rest 10 out of 24 patients vomited i.e. 41.6 treatments failed due non-adherence of guidelines.

In treatments with low to minimal emetogenic potential chemotherapy regimen (LEC) 15 of 30 was found significant.

As per study 93.3% Antiemetic regimens were inappropriate to emetogenic potential of chemotherapy regimen. 45.8% of antiemetic doses in regimen were insignificant. 27.2% administration errors were found. Here administration error is time gap between premedication antiemetics and chemotherapy which supposed to be at least 30 min and not more than 3.30 hours.

We have seen rare adverse drug reactions Extrapyrasidal symptoms, fatigue, sedation with Metoclopramide and Diarrhoea, headache with Ondansetron and also rare reaction extrapyramidal symptoms with promethazine. Extrapyrasidal symptoms in patients was seen during the being administered and found relieved after some time.

In treatments with AC regimen 48.8% were ondansetron. In PT regimen treatments 76% with combination of palonosetron, dexamethasone, Metoclopramide/promethazine. In TC regimen treatments two combinations were dominantly used i.e. Palonosetron+ dexamethasone 29.4% and Ondansetron + dexamethasone 35.2%. In Paclitaxel alone treatments combination antiemetics Palonosetron+ Dexamethasone ± Promethazine/Metoclopramide were used in 76% treatments. Intriguing part of this dissection is treatments Weekly CT cisplatin which is HEC and 50.9% were receiving mild antiemetic Metoclopramide of which 8 of 26 patients receiving Metoclopramide vomited i.e. 70% of treatments with Metoclopramide in Cisplatin weekly CT were found significant.

Despite of good antiemetic regimen, we have seen the patients vomiting or the experience of nausea this may because of overwhelmed emetic potential of chemotherapy regimen or Administration errors or Patient factors such as young age, female gender etc.

In our study we found NK 1 agonist with steroid found to be very effective in preventing vomiting but cost of the drug was limiting factor and 5HT3 antagonists except palonosetron and ondansetron other drugs were untouched, prochlorperazine was not considered for treatment and regimen containing anti-psychotics were not seen even in breakthrough and anticipatory emesis. Promethazine, Histamine receptor antagonist were not where recommended in guidelines but it being used widely in our practice hospital [6-16].

## Conclusion

The antiemetics used in CINV were not compliant with NCCN guidelines. However most of the treatments which were found non-compliant is justifiable with patients poor economic status or denial of government insurance to fund for Neurokinin 1 antagonist. Adherence to old guidelines especially in respect to dose was observed. some treatments were not adherent to guidelines but found effective in many patients on of such was use of Metoclopramide in cisplatin weekly CT and Inadequate education to nurses led to administration errors such as Time gap between premedication and chemotherapy which led to vomiting in around 27% of patients.

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## Bibliography

1. BS Sathvik. "Drug utilization review/evaluation". G. Parthasarathi, editors. A text book of clinical pharmacy practice. 1<sup>st</sup> edition. Chennai (IND): Orient Longman (2004): 362.
2. Cancer factsheet no 297 (2013).
3. AA Zeitoun. "Evaluation of anti-emetic use in chemotherapy-induced nausea and vomiting in a third-world country (Lebanon)". *Journal of Evaluation in Clinical Practice* 19.1 (2013): 68-75.
4. J Thomas, *et al.* "A comparison of oral delta-9- THC and prochlorperazine". *Cancer* 50.4 (1982): 636-645.
5. K Jordan. "Guidelines for antiemetic treatment of chemotherapy-induced nausea and vomiting: past, present, and future recommendations". *The Oncologist* 12.9 (2007): 1143-1150.

6. JW Gilmore. "Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in united states, community oncology practice: inspire study". *Journal of Oncology Practice* 10.1 (2014): 68-74.
7. PJ Hesketh. "Chemotherapy-induced nausea and vomiting". *New England Journal of Medicine* 358.23 (2008): 2482-2494.
8. S Schwartzberg. "Chemotherapy-induced nausea and vomiting: which antiemetic for which therapy?" *Oncology* 21.8 (2007): 946-962.
9. No. 9 obtained from cancer network.com.
10. K Garrett., *et al.* "Managing nausea and vomiting: current Strategies". *Critical Care Nurse* 23.1 (2003): 31-50.
11. TC Vicky and CF Yeo. "Antiemetic therapy options for chemotherapy induced nausea and vomiting in breast cancer patients". *Breast Cancer: Targets and Therapy* 3 (2011): 151-160.
12. BR Martin and JL Wiley. "Mechanism of action of cannabinoids: how It may lead to treatment of cachexia, emesis, and pain". *The Journal of Supportive Oncology* 2.4 (2004): 305-316.
13. EA Marty. "Comparison of 5 hydroxytryptamine<sub>3</sub> (serotonin) ondansetron with high dose of metoclopramide in control of cisplatin induced emesis". *New England Journal of Medicine* 322.12 (1990): 816-821.
14. T Grote and J Hajdenberg. "Combination therapy for chemotherapy-induced nausea and vomiting in patients receiving moderately emetogenic chemotherapy: palonosetron, dexamethasone, and aprepitant". *Oncology* 4.8 (2006): 403-408.
15. HJ Schmoll., *et al.* "Comparison of an aprepitant regimen with a multiple-day ondansetron regimen, both with dexamethasone, for antiemetic efficacy in high-dose cisplatin treatment". *Annals of Oncology* 17.6 (2006): 1000-1006.
16. National comprehensive cancer network. NCCN clinical practice guidelines in oncology: Anti Emesis. Volume 1 (2013).

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