Drug Utilisation Evaluation of Antiemetic Drugs Used as Prophylaxis for Chemotherapy Induced Nausea and Vomiting and Evaluation of WHO Core Prescribing Indicators in Tertiary Care Hospital

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www.ijppr.humanjournals.com

Keywords: Antiemetics, CINV, Cancer, Dexamethasone, WHO Prescribing Indicators

ABSTRACT

Objectives: The objective of this study was to analyse the drug utilisation pattern of antiemetics used as prophylaxis for chemotherapy induced nausea and vomiting and to evaluate the prescription pattern using WHO core prescribing indicators. Methods: This study was a prospective observational study conducted in oncology department at Muthoot health care hospital Pvt Ltd., Kozhencherry, Pathanamthitta, Kerala. A sample size of 200 patients was enrolled after obtaining the consent, then evaluated the prescription pattern, dose, frequency and effect of antiemetics used. The prescription pattern of oncology department was also analysed using WHO core prescribing indicators. Results: Among 200 subjects enrolled in this study, corticosteroid class of antiemetics and selective 5-HT3 antagonist are more frequently prescribed followed by NK1 receptor antagonist for the prevention of chemotherapy induced nausea and vomiting. Dexamethasone was the most commonly prescribed antiemetic drug (49.1%), followed by Ondansetron (25.8%), Palanosetron (13.5%), Granisetron (9.7%), Aprepitant (1.6%). Analysis using WHO prescribing indicators showed that prescription was according to WHO core prescription indicators. Conclusion: From this study, we could conclude that corticosteroid class of antiemetics and selective 5-HT3 antagonist are more frequently prescribed followed by NK1 receptor antagonist for the prevention of chemotherapy induced nausea and vomiting. WHO prescribing indicators can be used as an effective tool to analyse the prescription pattern of drugs.

INTRODUCTION

Cancer has a prominent place among major health concerns of society. The cancer incidence rate in India increased by 63.4 per 100,000 in 1990 to 81.2 per 100 000 in 2016. Cancer incidence rates and were highest in Kerala (135.35 per 100,000) and Mizoram (121.7 per100, 000)[1]. Chemotherapy involves the use of drugs to destroy cancer cells. It works by destroying cancer cells that grow rapidly. Unfortunately, chemotherapy also affects normal cells that grow rapidly, such as blood cells forming in the bone marrow, cells in the hair follicles or cells in the mouth and intestines. The side-effects of anti-cancer chemotherapy remain a major source of concern for both clinicians and patients even with the enhanced survival and improved efficacy offered by modern treatments. Current drugs or other approaches to counteract chemotherapy-induced adverse effects are often incompletely effective, frequently do not address potential long term consequence or may even cause other side-effects which only increases the patient discomfort[5].

Nausea and vomiting are still among the most common, expected, and feared side effects among patients receiving chemotherapy. In fact, some cancer patients delay chemotherapy treatments and refuse future treatments due to chemotherapy-induced nausea and vomiting (CINV) experienced by them.[6] CINV is commonly classified as acute, delayed, anticipatory, breakthrough or refractory.[7] Anticipatory nausea and vomiting are also problems among chemotherapy patients.[6] The incidence and severity of nausea and/or vomiting in patients receiving chemotherapy is determined by numerous factors including:

- The specific therapeutic agents used.

- Dosage of the agents

- Schedule and route of administration of the agents

- Individual patient variability (age, sex, prior chemotherapy)

More than 90 % of patients receiving highly emetogenic chemotherapy (HEC) have episodes of vomiting. However, if patients receive prophylactic antiemetic regimens before treatment with HEC, then vomiting reduces to 30%.[7]

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Vomiting results from stimulation of a multistep reflex pathway controlled by the brain. It trigger zone (CTZ), cerebral cortex, pharynx and gastrointestinal (GI) tract. It occurs when efferent impulses are sent from the vomiting centre (VC) to the salivation centre, abdominal muscles, respiratory center and cranial nerves. The CTZ, VC and GI tract have many neurotransmitter receptors. Activation of these receptors by chemotherapeutic agents is responsible for chemotherapy induced emesis. The important neuroreceptors involved in emesis are serotonin (acute emesis) and dopamine receptors. Other neuroreceptors involved in emesis include acetylcholine, histamine, opioid, neurokinin-1 (NK1) receptors. NK1 receptors are associated with delayed emesis. Antiemetic agents can exert their effects at different points during the course of emesis, block different neuronal pathways, or behave synergistically with other antiemetic agents to potentiate an antiemetic effect. Antiemetic therapy should be initiated before chemotherapy to provide maximal protection against chemotherapy induced emesis. It should also be continued for the same duration of time as the emetic activity of the chemotherapeutic agent being used.

Class of antiemetics includes:

- Serotonin (5-HT3) Antagonists: ondansetron, granisetron, dolasetron, palonosetron

- Neurokinin -1-Receptor Antagonists: aprepitant, fosaprepitant, rolapitant, netupitant

- Other Antiemetics: dexamethasone

Based on the emetic risk of the chemotherapeutic agent, previous experience with antiemetics, and patient specific risk factors, antiemetic regimens should be chosen. Patients need to be protected throughout the entire period of risk, which lasts for at least 3 days for high emetic risk agents and 2 days for moderate emetic risk agents after the last dose of anti cancer therapy.[7]

Drug use is a complex process since optimal benefits of drug therapy in patient care may not be achieved because of under-use, overuse or misuse of these drugs. Inappropriate drug use may also lead to adverse effects, increased cost of medical care, and patient mortality. Hence, in recent years, Drug Use Evaluation (DUE) studies have become a potential tool to be used in the evaluation of health care systems.

DUE studies are defined as the study of marketing, distribution, prescription and use of drugs

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in a society, with special emphasis on the resulting medical, social and economic consequences. DUE provide an insight of the efficacy and pattern of drug use and the quality and outcome of use.[2] Core prescribing indicators developed by World Health Organization (WHO) (table:1) is a tool which aids to review the prescribing pattern. It measures the degree of polypharmacy, the tendency to prescribe drugs by generic name and the overall level of use of injections. The degree to which the prescribing practice conformed to the Essential Drug List and formulary is also measured by searching for the number of drugs prescribed from essential drug list available.[21]

TABLE No. 1: WHO PRESCRIBING INDICATORS

Number of drugs per prescription
Percentage (%) of encounters with an antibiotic prescribed.
Percentage (%) of encounters with a cytotoxic injectable.
Number of encounter with injectable
Average number of cytotoxic drugs per prescription.
Percentage(%) of drug prescribed by generic name
Percentage(%) of drugs from WHO model list
Percentage of drugs prescribed from EDL
Percentage (%) of drugs prescribed from hospital formulary

This present study aimed to analyze and evaluate the trends and patterns of prescribing anticancer drugs. It also aimed to provide a review of prescribing practices to physicians, which aim for better healthcare delivery. WHO core prescribing indicators (see table 1)was compiled at the end of the study to know the amount of prescriptions with polypharmacy, percentage of prescriptions with injectable and antibiotics, percentage of drugs prescribed from Essential Drugs list etc.

METHODS

This study was a prospective observational study done in Muthoot health care hospital Pvt Ltd kozhenchery. Our sample size was 200 and for a duration of 6 months. After getting approval from IRB committee, a written Informed Consent printed in their understandable language was obtained from the patient or care-giver, if the subject was unable to give the same; it was obtained from the legal representative. Patients between the age group of 18-90,

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both gender, IP and OP patients undergoing chemotherapy was chosen for the study A detailed description about the study, regarding its confidentiality, objectives, implications in the society were given to each patient. The data regarding use of antiemetics were collected from the respective patient profile and then analyzed by Microsoft excel.

RESULTS

Among 200 subjects enrolled in this study, corticosteroid class of antiemetics and selective 5-HT3 antagonist are more frequently prescribed followed by NK1 receptor antagonist for the prevention of chemotherapy induced nausea and vomiting.

TABLE 2: THERAPEUTIC CLASSWISE PRESCRIBING PATTERN OF ANTIEMETICS

SL. NO	CLASS OF ANTIEMETICS IN CINV	DRUGS	FREQUENCY	PERCENTAGE
1	Corticosteroids	Dexamethasone	116	49.1
2	Selective 5-HT$_3$ Antagonist	Ondansetron	61	25.8
		Granisetron	23	9.7
		Palanosetron	32	13.5
3	Neurokinin 1 Receptor Antagonist	Aprepitant	4	1.6
	Total		236	100
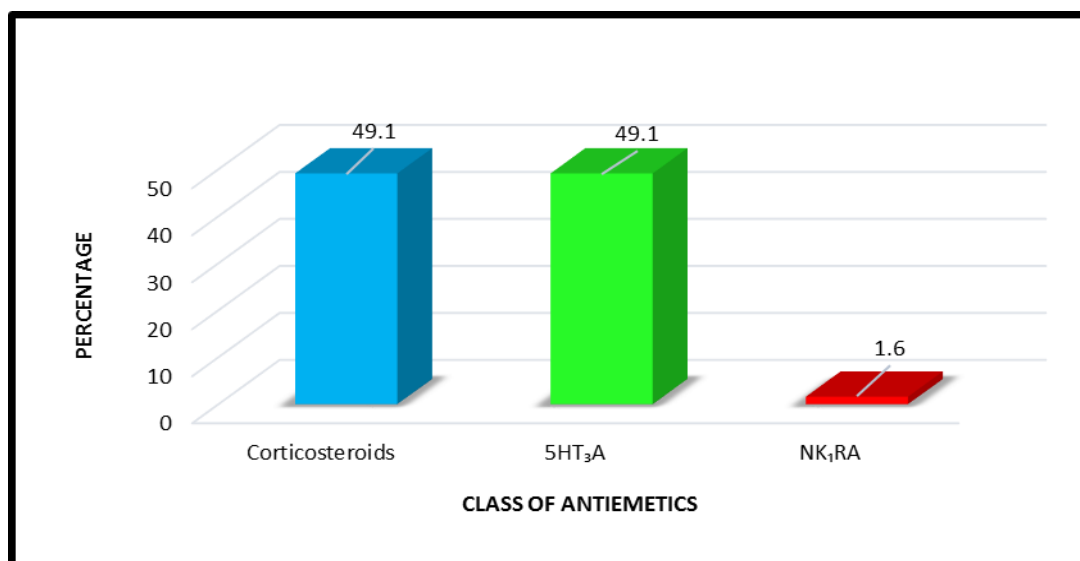
FIGURE No. 1: THERAPEUTIC CLASSWISE PRESCRIBING PATTERN OF ANTIEMETICS

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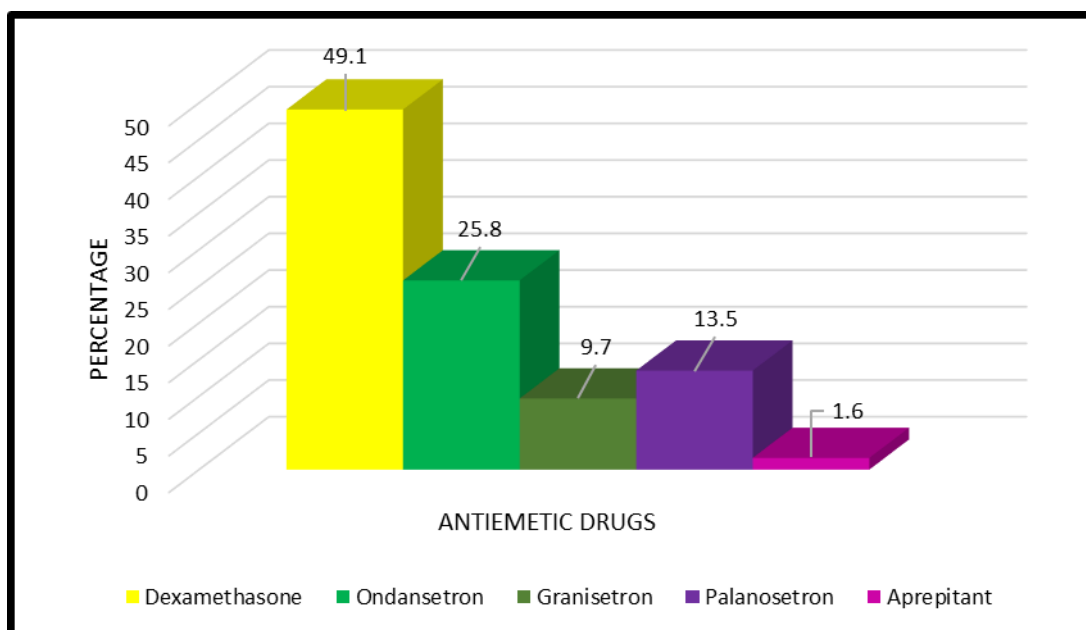
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FIGURE No. 2: DRUG WISE DISTRIBUTION OF ANTIEMETICS

Dexamethasone was the most commonly prescribed antiemetic drug (49.1%), followed by Ondansetron (25.8%), Palanosetron (13.5%), Granisetron (9.7%), Aprepitant (1.6%).

TABLE No. 3: WHO PRESCRIBING INDICATORS

Number of drugs per prescription	8.1
Percentage (%) of encounters with an antibiotic prescribed.	45%
Percentage (%) of encounters with a cytotoxic injectable.	71.5%
Number of encounter with injectable	100
Average number of cytotoxic drugs per prescription.	1.5%
Percentage(%) of drug prescribed by generic name	47.8%
Percentage(%) of drugs from WHO model list	95%
Percentage of drugs prescribed from EDL	95%
Percentage (%) of drugs prescribed from hospital formulary	97%

WHO prescribing indicators showed that number of drugs per prescriptions was found to be 8.1. Percentage of encounters with an antibiotic prescribed was 45%. Percentage of encounters with a cytotoxic injectable was 71.5%. Average number of cytotoxic drugs per prescription was 1.5%. Number of encounters with injectable was 100%. Percentage of drugs prescribed with generic name was 47.8%. Percentage of drugs from WHO model list was 95%. Percentage of drugs prescribed from EDL was 95%. Percentage of drugs prescribed

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from hospital formulary was 97%.

DISCUSSION

PRESCRIPTION PATTERN OF ANTIEMETIC DRUGS

According to our findings, corticosteroids, 5-HT3 receptor blockers and NK1 receptor blockers are the most commonly prescribed classes of antiemetics. Dexamethasone was the most commonly prescribed antiemetic drug (49.1%), followed by Ondansetron (25.8%), Palanosetron (13.8%), Granisetron (9.7%), and Aprepitant (1.6%). This result is consistent with the findings from other articles. Study conducted by **Gruenberg S M**[39] concluded that the most frequently employed antiemetic agents include corticosteroids [methylprednisolone, dexamethasone], serotonin type 3 (5-HT3) receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron, palonosetron), and neurokinin-1 (NK1) receptor antagonists (aprepitant). According to study conducted by **BaburajG**[28]**,** dexamethasone is prescribed in combination with aprepitant followed by palonosetron and in our study dexamethasone is used in combination with palonosetron and granisetron which belongs to 5-HT3 receptor blocker classification. Dexamethasone is the most preferred antiemetic drug for preventing CINV. Dexamethasone can be used as both monotherapy and in combination with older and recently developed antiemetic agents for preventing acute and delayed emesis induced by chemotherapy.

WHO PRESCRIBING INDICATORS

According to WHO core prescribing indicators in our study, Number of drugs per prescriptions was found to be 8.1. Percentage of encounters with an antibiotic prescribed was 45%. Percentage of encounters with a cytotoxic injectable was 71.5%. Average number of cytotoxic drugs per prescription was 1.5%. Number of encounters with injectable was 100%. Percentage of drugs prescribed with generic name was 47.8%. Percentage of drugs from WHO model list was 95%. Percentage of drugs prescribed from EDL was 95%. Percentage of drugs prescribed from hospital formulary was 97%.

According to **Mugada V *et al.*,**[21] Average number of Cytotoxic Drugs per prescription was 1.97. Average number of drugs per prescription was 8.16. Percentage of drugs prescribed from Essential Drugs List was 88.4%. This study is consistent with our study except in case of percentage of drugs prescribed from WHO mode list and Essential drug list. The average

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number of drugs per prescription in our study is 8.1. This higher percentage is because of other supportive medications like antiemetics, proton pump inhibitors, and antibiotics which are prescribed as pre medications for preventing CINV and also to treat various infections in immune compromised patents. So it cannot be explained as polypharmacy. The antibiotic prescription was also rational since it was limited to various infections caused by immune suppression as a result of chemotherapy. The drug prescribed from hospital formulary and was on and on a nonprofit basis.

CONCLUSION

Many effective treatment modalities are available now to treat effectively cancer As part of the treatment, subjects experienced many side effects such as CINV and myleo suppression. In order to prevent CINV, antiemetics such as corticosteroids, 5HT3 receptor blockers and NK1 receptor blockers were prescribed. Dexamethasone was the most commonly prescribed antiemetic drug. Analysis of drug utilisation of anticancer drugs is of great importance in current scenario. A WHO prescribing indicator is an effective tool to assess the drug utilization pattern. According to our study, most of the drugs prescribed were from hospital formulary and in accordance with EDL according to WHO prescribing indicators. The prescribing pattern of anticancer drugs needs to be continuously evaluated. It helps in therapeutic decision making and promoting the effective, non-profit based drug therapy which can improve patient satisfaction by providing expected therapeutic outcome.

CONFLICT OF INTEREST

FUNDING

ACKNOWLEDGEMENT

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