Research Paper

Effectiveness of Antiemetics in the Management of Chemotherapy-induced Nausea and Vomiting in Cancer Patients Following Chemotherapy Guidelines

GEETHA KANDASAMY, P. SIVANANDY[1], M. KHOBRANI, DALIA ALMAGHASLAH, MONA ALMANASEF, RAJALAKSHIMI VASUDEVAN, MAHESWARI CHINNADHURAI[2], NAYANA HONEY[3]

Department of Clinical Pharmacy, College of Pharmacy, King Khalid University, Abha-61441, Kingdom of Saudi Arabia, [1]Department of Pharmacy Practice, School of Pharmacy, International Medical University, Kuala Lumpur, Malaysia, [2]Department of Pharmacy Practice, College of Pharmacy, Shaqra University, Al- Dawadmi Campus, Kingdom of Saudi Arabia, [3]Department of Pharmacy Practice, KMCH College of Pharmacy, Coimbatore-641 048, India

Cancer chemotherapy might in turn induce nausea and vomiting as a side effect, which impairs patients' quality of life and adherence to medications. Inconsistent following of antiemetic guidelines among the physician could significantly increase the incidence of chemotherapy-induced nausea and vomiting in cancer patients. This study was aimed to evaluate antiemetic guidelines consistency and the effectiveness of antiemetics in controlling chemotherapy-induced nausea and vomiting in cancer patients. This study was carried out among patients treated with low emetogenic chemotherapy to highly emetogenic chemotherapy who had completed their first chemotherapy cycle at the department of Haemato-Oncology. Among the 1725 adult patients enrolled in the study, only 60 % received cancer medications according to the standard guidelines and 40 % did not. Fifty-two percent patients were under highly emetogenic chemotherapy regimen, 36 % were in moderate emetogenic chemotherapy and 12 % in low emetogenic chemotherapy regimen. Antiemetic drug was given adjunct to cancer chemotherapy, in which 82 % of patients were found to have no emesis in all highly emetogenic chemotherapy, moderate emetogenic chemotherapy and low emetogenic chemotherapy cohorts while 8.35 % with acute, 7.65 % with delayed, 2.32 % with acute and delayed emesis were observed in highly emetogenic chemotherapy cohort. A 10 % failure rate was observed in the treatment groups even though the guidelines were followed to treat chemotherapy-induced nausea and vomiting. In addition to implementing anticancer treatment guidelines, strict monitoring of patients and follow up is very essential to prevent treatment failure in chemotherapy-induced nausea and vomiting.

Key words: Oncology, chemotherapy, supportive care, malignancy, antiemetics, guidelines

Cancer (malignancy) is a common term for the group of more than 150 diseases characterized by uncontrolled growth and spread of abnormal cells[1]. There are more than 100 types of cancer and the types of cancer are determined by what type of cells begins to grow abnormally and where in the body the abnormal growth occurs, e.g., breast cancer, lung cancer, colon cancer, rectal cancer, endometrial cancer, ovarian cancer, prostate cancer, and skin cancer. Symptoms of cancer depend upon the specific type and of cancer. Treatments of cancer are chemotherapy, radiation and surgery[2]. The main causes of cancers are tobacco usage, obesity, diet, lack of physical activity, alcohol, infections (20 %) such as hepatitis B, C, human papilloma virus, exposure to ionizing radiation, pollutants and partly by changing the genes of cell[3].

According to the American Cancer Society, there are seven warning signs of cancer that has to be monitored carefully for the early diagnosis of cancer, it includes change in bowel habits, a sore that does not heal, unusual discharge or bleeding, thickening or lump in the breast or elsewhere, change in digestion, or difficulty in swallowing, apparent change in a mole and distressing cough[1,4]. The common symptoms of cancer are fatigue, anorexia, weight loss, anemia, marked

***Address for correspondence**
E-mail: geethpharma@gmail.com

Accepted 26 June 2019
Revised 30 March 2019
Received 24 December 2018
Indian J Pharm Sci 2019;81(4):757-765

weakness, alterations in taste perception, leucopenia, thrombocytopenia, and infection[1].

In cancer management, early diagnosis and start of cancer treatment are warranted. There are several drugs discovered and available for the treatment of different cancer types, however some drugs are preferred to use as monotherapy and some are used along with other agents as combination therapy. Some drugs are given orally and some are given by the intravenous (iv) route. Example for drugs that are given as a single iv injection are cisplatin, dacarbazine, carmustine, mechlorethamine, streptozotocin, oxaliplatin, cytarabine, carboplatin, ifosfamide, doxorubicin, daunorubicin, docetaxel, paclitaxel, mitoxantrone, etoposide, topotecan, 5-fluorouracil and methotrexate; and as a single oral dose are procarbazine, hexamethylmelamine cyclophosphamide, vinorelbine, etoposide, capecitabine, and fludarabine[5-7].

Chemotherapy-induced nausea and vomiting (CINV) is the most feared common side effect linked with cancer therapy[8]. Nausea is an unlikable wave like symptom occur in the back of the throat and or the epigastria that may wind up in vomiting. Vomiting is a self-limited, short-lived, persuasive expulsion of the contents present in stomach, duodenum and jejunum through oral cavity[9]. More than 80 % patients who receive cancer chemotherapy experience nausea and vomiting (NV). CINV adversely affects patients quality of life (QoL), causes serious metabolic complications, and leads to poor compliance to anticancer regimen[10].

Frequent vomiting associated with cancer chemotherapy causes loss of body fluids and electrolyte imbalance. CINV also reduces the tendency to eat or drink anything, and affect physical, emotional and social wellbeing of cancer patients[11]. If this condition continues it might cause fatigue, anxiety, lack of concentration, impairment of wound healing, weight loss, lack of appetite and it would became a serious health problem very quickly[12,13].

Several classifications of CINV are widely used including acute, delayed, anticipatory, breakthrough and refractory. Acute CINV starts during the first 24 h, usually within the first few minutes to hours after the administration of chemotherapy. Delayed CINV develops in patients 24 h after the administration of chemotherapy. It may continue up to 6 d and it commonly occurs with cisplatin, carboplatin, cyclophosphamide and anthracyclines. Anticipatory NV starts in patients before receiving chemotherapy due to a prior adverse experience with chemotherapy. Breakthrough CINV occurs despite prophylactic treatment. Refractory NV occur throughout subsequent cycles of chemotherapy when antiemetic prophylaxis is unsuccessful in earlier cycles. The different grading of CINV and the risk category of anticancer drugs are presented in Tables 1[13] and 2[14], respectively.

Based on this risk criterion there are specific strategies available under chemotherapy guidelines. There are several guidelines commonly used nowadays, such as the National Comprehensive Cancer Network (NCCN), the American Society of Clinical Oncology (ASCO), the Multinational Association of Supportive Care in Cancer (MASCC) and the European Society for Medical Oncology. These guidelines are given in Tables 3[15-17] and 4[18,19].

In various hospitals, different antiemetic guidelines are followed and proper utilization of these guidelines in hospitals is evaluated through drug utilization methods. Drug utilization evaluation (DUE) is a potential, ongoing, and systematic tool for the critical evaluation of utilization of drug(s) and to ensure that the medicines are used appropriately and rationally. It can be used to provide early signals of irrational and misuse of drugs, also used to enhance the appropriate use of drugs, improvement in quality control cycle and its continuous quality improvement[20-22].

DUE can provide adequate insight into the rational use of drugs and can increase the awareness of how drugs are being used to treat various diseases. DUE is most meaningful in continuous evaluation system and when it is followed over a period of time, trends in drug use can be recognised[20]. Researchers can estimate

TABLE 1: GRADING OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING[13]

	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition; iv fluids indicated for less than 24 h	Inadequate oral caloric or fluid intake; iv fluids, tube feeding or TPN indicated for >2 h	Life-threatening consequences	Death
Vomiting	1 episode in 24 h	2-5 episodes in 24 h; iv fluids indicated for less than 24 h	>6 episodes in 24 h; iv fluids or TPN indicated for >24 h	Life threatening consequences	Death

the rational, overuse and misuse of drugs and or alternatives, and the extent of drugs use. It can be used to analyze and compare utilization pattern of drug(s) for the treatment of disease(s) with current guidelines and recommendations. Inconsistent use with reference to guideline recommendations in treating disease

TABLE 2: RISK CATEGORY OF ANTICANCER DRUGS[14]

High risk	Moderate risk	Low risk	Minimal risk
Carmustine Cisplatin Cyclophosphamide Dacarbazine Mechlorethamine	Alemtuzumab Azacitidine Bendamustine Carboplatin Clofarabine Cyclophosphamide Cytarabine Daunorubicin Doxorubicin Epirubicin Idarubicin Cyclophosphamide Imatinib Temozolomide Vinorelbine Ifosfamide Irinotecan Oxaliplatin	Bortezomib Cabazitaxel Catumaxomab Cetuximab Cytarabine Docetaxel Doxorubicin (liposomal) Etoposide 5-Fluorouracil Gemcitabine Ixabepilone Paclitaxel	Bevacizumab Chlorambucil Bleomycin Erlotinib Busulfan Gefitinib Cladribine Hydroxyurea Vinorelbine Fludarabine Rituximab Vinblastine Vincristine Mustard Methotrexate Sorafenib

High risk- nearly always causes nausea and vomiting, moderate risk- usually causes nausea and vomiting, low risk- sometimes causes nausea and vomiting and minimum risk- rarely causes nausea and vomiting

TABLE 3: NCCN AND ASCO ANTIEMETIC GUIDELINES[15-17]

Emetic-risk Category	ASCO guidelines	NCCN Guidelines
High (>90 %) risk	Three-Drug combination of $5HT_3$ receptor antagonist, dexamethasone, and aprepitant recommended before chemotherapy	Before chemotherapy, a $5HT_3$ receptor antagonist (ondansetron, granisetron, dolasetron or palonosetron*) dexamethasone 12 mg and aprepitant (125 mg) recommended, with or without lorazepam
	For patients receiving cisplatin and all other agents of high emetic risk, the two drug combination of dexamethasone and aprepitant recommended for prevention of delayed emesis	For prevention of delayed emesis, dexamethasone (8 mg) on days 2-4 plus aprepitant (80 mg) on days 2 and 3 recommended, with or without lorazepam on days 2-4
	For patients receiving an anthracycline and cyclophosphamide, the three drug combination of a $5HT_3$ receptor antagonist, and dexamethasone, and aprepitant recommended before chemotherapy; single agent aprepitant recommended on days 2 and 3 for prevention of delayed emesis	For patients receiving an anthracycline and cyclophosphamide and selected patients receiving other chemotherapies of moderate emetic risk (e.g., carboplatin, cisplatin, doxorubicin, epirubicin, ifosfamide, irinotecan, or methotrexate), a $5HT_3$ receptor antagonist (ondansetron, granisetron, dolasetron or palonosetron*) dexamethasone (12 mg) and aprepitant (125 mg) recommended, with or without lorazepam, before chemotherapy; for other patients, aprepitant is not recommended
Moderate (30 % to 90 %) risk	For patients receiving other chemotherapies of moderate emetic risk, the two drug combination of a $5HT_3$ receptor antagonist, and dexamethasone recommended before chemotherapy; single agent dexamethasone or a $5HT_3$ receptor antagonist suggested on days 2 and 3 for prevention of delayed emesis	For prevention of delayed emesis, dexamethasone (8 mg) or a $5HT_3$ receptor antagonist on days 2-4 or, if used on day 1, aprepitant (80 mg) on days 2 and 3 with or without dexamethasone (8 mg) on days 2-4, recommended, with or without lorazepam on days 2-4
Low (10-30 %) risk	Dexamethasone (8 mg) suggested; no routine preventive use of antiemetics for delayed emesis suggested	Metoclopramide, with or without diphenhydramine; dexamethasone (12 mg); or prochlorperazine recommended, with or without lorazepam
Minimal (<10 %) risk	No antiemetic administered routinely before or after chemotherapy	No routine prophylaxis; consider using antiemetics listed under primary prophylaxis as treatment

NCCN: National Comprehensive Cancer Network, ASCO: American Society of Clinical Oncology

TABLE 4: MASCC/ESMO ANTIEMETICS GUIDELINE[18,19]

Group	High		Moderate		Low		Minimal	
	Acute CINV	Delayed CINV	Acute CINV	Delayed CINV	Acute CINV	Delayed CINV	Acute CINV	Delayed CINV
MASCC	5-HT_3RA +dexamethasone +aprepitant	Dexamethasone +aprepitant	Anthracycline/ cyclophosphamide 5-HT_3RA+dexamethasone +aprepitant Other than anthracycline/ cyclophosphamide 5-HT_3RA+dexamethasone +aprepitant	Aprepitant or dexamethasone Dexamethasone, 5-HT_3RA may be used as an alternative	Dexamethasone	a	a	a

5-HT_3RA- 5-hydroxytryptamine receptor antagonist; a- as required, MASCC: Multinational Association of Supportive Care in Cancer, ESMO: European Society for Medical Oncology

might adversely affect patients' QoL and also cause huge economic burden[22]. Hence, this study was aimed to evaluate the antiemetic guidelines consistency and the effectiveness of antiemetics in controlling CINV in cancer chemotherapy patients.

MATERIALS AND METHODS

A study was carried out in chemotherapy patients who had completed their first chemotherapy cycle in the department of haemato-oncology of an 800 bed teaching hospital from September 2016 to August 2018. A total of 1725 patients who received antiemetics along with cancer chemotherapy were included in this study after obtaining their informed consent. Patients receiving both chemo and radiation therapy were excluded from the study.

Study protocol:

The study participants were categorized into 2 groups, the guideline-consistent chemotherapy prophylaxis group (GCCP) and the guideline-inconsistent chemotherapy prophylaxis group (GICP) where patients received antiemetic prophylaxis as per the standard guidelines to control CINV. Further, based on the emetogenicity of chemotherapy regimen given, three groups were created, highly emetogenic chemotherapy (HEC), moderately emetogenic chemotherapy (MEC) and low emetogenic chemotherapy (LEC). For analysing emesis in cancer patients, the study group was categorized into those with acute emesis, delayed emesis, acute and delayed emesis, and no emesis. The study participant's data were collected from the oncology department. Data were transferred directly from the patient case sheets, treatment records and direct interview with the patients. Specially designed data entry form was used to collect patient's demographics, type of cancer regimen, antiemetics given and its emetogenicity, details of patient's NV frequency and its grading, comparison of the data with standard guidelines, failure rate of antiemetics. This study included all patients those who were undergoing low to high emetogenic chemotherapy regardless of the type of solid tumors. The intensity and severity of NV experienced by the patients in all types of emesis were recorded with the aid of nausea grading as well as NCCN, MASCC and ASCO guidelines. Statistical analysis was performed and the individual variables were expressed as percentages. The study proposal and methodology was approved by Institutional Ethics Committee wide number EC/AP/372/03/2015.

RESULTS AND DISCUSSION

This prospective study was aimed to evaluate antiemetic guidelines consistency and the effectiveness of antiemetics in controlling CINV in cancer chemotherapy patients. A total of 2400 cancer patients were admitted to the hospital for their treatment during the study period. Out of this, 675 patients were receiving both chemo and radiation therapy and were excluded from the study. Out of 1725 patients enrolled in the study, 914 (53 %) were female and 811 (47 %) were male. Sixty percent (n=1035) patients were given the medication according to standard guidelines and 40 % (n=690) were not (Table 5). Regarding the emetogenic potential of the chemotherapy regimen, 52 % (n=897) patients were in HEC, 36 % (n=621) patients in the MEC and the remaining 12 % (n=207) patients were in LEC regimen. Among those patients received both chemotherapy and antiemetics, most of the patients (n=1409; 81.68 %) were found without emesis, 8.35 % (n=144) were with acute emesis, 7.65 % (n=132) were in delayed emesis, 2.32 % (n=40) were both in acute and delayed emesis. Based on nausea grading, 8.29 % (n=143) of the study population had

grade-1 nausea, 4.35 % (n=75) grade-2 nausea, 3.01 % (n=52) grade-3 and 2.67 % (n=46) experienced grade-4 nausea, however 81.68 % (n=1409) did not report any nausea. Readmission to the hospital with complaints of nausea or vomiting within a week was considered as the failure of therapy. In this study, 10 % (n=173) of patients fall under failure of therapy and 90 % (n=1552) in no failure of therapy group. The details are presented in Table 5.

The total population was categorized into two groups as GCCP and GICP groups. Among 1725 patients enrolled, 552 (32 %) female and 483 (28 %) male were compliant to the standard treatment guidelines while 362 (21 %) female and 328 (19 %) male patients were noncompliant to these standard guidelines. As per the emetogenicity of cancer chemotherapy, among the HEC group 518 (30 %) patients fall in GCCP and 379 (21.97 %) were fall in GICP group. In case of MEC and LEC, the patients complied with chemotherapy guidelines were 356 (20.64 %) and 161 (9.33 %), respectively, whereas in the noncompliant group it was 265 (15.36 %) and 46 (2.67 %), respectively.

Comparing the guideline compliance with the type of emesis, 23 (1.33 %) patients in the GCCP and 121 (7.01 %) patients in GICP showed acute emesis, 17 (0.99 %) patients in GCCP and 115 (6.67 %) in GICP group had delayed emesis, whereas 6 (0.35 %) patients in GCCP and 34 (1.97 %) patients in GICP had acute and delayed emesis. Most of the patients who did not complained of emesis included 989 (57.33 %) in GCCP and 420 (24.35 %) in GICP groups. On comparing the failure rate and guideline consistency, the study showed that 9.68 % (n=167) patients in GICP and only 0.35 % (n=6) in GCCP were readmitted to the hospital with complaints of second grade to fourth grade nausea or vomiting. However, most (n=1029; 59.65 %) of the GCCP patients have not had readmission to the hospital with any vomiting complaints. The details are presented in Table 6.

Among the 782 (45.33 %) patients who received HEC alone, 144 (8.35 %) received monotherapy and 638 (36.98 %) received combination therapy. In monotherapy, dacarbazine, cisplatin and cyclophosphamide were prescribed to 52, 75, and 17 patients, respectively. In combination therapy, cisplatin plus dacarbazine and cisplatin plus cyclophosphamide plus dacarbazine were given in 201 (11.65 %) and 437 (25.34 %) patients, respectively. One hundred and fifty (8.69 %) patients received both HEC

TABLE 5: DISTRIBUTION OF STUDY POPULATION

Group	Number of patients (n=1725)	Percent
Gender:		
Male	811	47.01
Female	914	52.99
Guideline consistency:		
Guideline consistent chemotherapy prophylaxis	1035	60
Guideline inconsistent chemotherapy prophylaxis	690	40
Emetogenicity:		
Highly emetogenic chemotherapy	897	52
Moderately emetogenic chemotherapy	621	36
Low emetogenic chemotherapy	207	12
Types of emesis received:		
Acute	144	8.35
Delayed	132	7.65
Acute and delayed	40	2.32
No emesis	1409	81.68
Nausea grading among the study population:		
Grade 1	143	8.29
Grade 2	75	4.35
Grade 3	52	3.01
Grade 4	46	2.67
No nausea	1409	81.68
Failure rates:		
Yes	173	10.03
No	1552	89.97

Failure meaning antiemetics readministered within one week

TABLE 6: DISTRIBUTION OF STUDY POPULATION BASED ON GUIDELINES CONSISTENCY (n=1725)

Category	Groups, number of patients (%)	
	GCCP, 1035, (60 %)	GICP, 690, (40 %)
Gender:		
Male	483 (28.00)	328 (19.01)
Female	552 (32.00)	362 (20.99)
Emetogenicity:		
HEC	518 (30.03)	379 (21.97)
MEC	356 (20.64)	265 (15.36)
LEC	161 (9.33)	46 (2.67)
Types of emesis:		
Acute	23 (1.33)	121 (7.01)
Delayed	17 (0.99)	115 (6.67)
Acute and delayed	6 (0.35)	34 (1.97)
No emesis	989 (57.33)	420 (24.35)
Failure rates:		
Yes	6 (0.35)	167 (9.68)
No	1029 (59.65)	523 (30.32)

HEC- Highly emetogenic chemotherapy, MEC- moderately emetogenic chemotherapy LEC- low emetogenic chemotherapy, failure is antiemetics readministered within one week

and MEC concurrently, which was cyclophosphamide plus doxorubicin. Five hundred and forty-six (31.65 %) patients received MEC as monotherapy, among these 115 (6.67 %) patients received doxorubicin, 310 (17.97 %) received carboplatin and 121 (7.01 %) received oxaliplatin. There were 58 (3.36 %) patients received both HEC and LEC as combination therapy, which was cyclophosphamide plus methotrexate. Moreover, 189 (10.96 %) patients received LEC as monotherapy, among them 104 (6.03 %) patients received paclitaxel, 34 (1.97 %) each received docetaxel and gemcitabine and 17 (0.99 %) received methotrexate. The details are given in Table 7.

There were group of antiemetics given to control the CINV. Among the 1725 patients, 730 (42.32 %) received 3 antiemetics, 788 (45.68 %) received 2 antiemetics as combination therapy and 207 (12 %) received an antiemetic as monotherapy. Five hundred and forty (31.31 %) patients received palonosetron+dexamethasone+aprepitant, 270 (15.65 %) patients received palonosetron+dexamethasone, 190 (11.01 %) received dexamethasone+palonosetron+olanzapine, whereas 518 (30.03 %) patients received dexamethasone+ondansetron combination. Moreover, 161 (9.33 %) patients received dexamethasone and only 46 (2.67 %) received ondansetron as monotherapy. The details of antiemetics prescribed are presented in Table 8.

CINV has a major impact on the daily lives of cancer patients and causes serious harm to the body. The failure of antiemetic therapy will adversely affect the patients QoL. CINV can be prevented or reduced by using appropriate antiemetic therapy. The most important factors that determine the effect of antiemetics in CINV are narrow patient selection, well-defined protocol-based chemotherapy, and suitable antiemetic regimen.

Since 1960s, studies of antiemetics in cancer patients have been a great field of medical research, but CINV is still a major issue in cancer patients. Substantial progress in the understanding of the mechanism of CINV stimulated the researchers to develop new antiemetics such as antidopaminergics, corticosteroids, 5-HT3 receptor antagonists (5-HT3RA), NK1 receptor antagonists and also the new antipsychotic agent olanzapine. Development of these drugs has led to the establishment of numerous international guidelines for the prevention and treatment of CINV[23].

In this prospective observational study, patients were evaluated after their first chemotherapy cycle to assess the efficacy and outcome of antiemetics to reduce CINV. A total of 1725 patients received anticancer chemotherapy and among them HEC (n=897; 52 %) was given to a majority of patients followed by MEC (n=621; 36 %), and LEC (n=207; 12 %) chemotherapy.

In this study, majority of the participants were female (n=914, 53 %), which is similar to the studies reported by De Tursi *et al.*[24] and Elizabeth *et al.*[25] in which female participants were 65 and 79 %, respectively. In the gender wise distribution of cancer, female cancer patients are more due to their lifestyle and food habits, which led to breast and cervical cancer. In this study most of the patients were treated with

TABLE 7: COMMONLY PRESCRIBED CHEMOTHERAPY IN THE STUDY POPULATION

Emetogenicity	Name of chemotherapy	Number of patients (n=1725)	Percent
High emetogenic chemotherapy	Dacarbazine	52	3.01
	Cisplatin	75	4.35
	Cisplatin plus dacarbazine	201	11.65
	Cisplatin+ cyclophosphamide+dacarbazine	437	25.34
High and moderate emetogenic chemotherapy	Cyclophosphamide	17	0.99
	Cyclophosphamide+doxorubicin	150	8.69
Moderate emetogenic chemotherapy	Doxorubicin	115	6.67
	Carboplatin	310	17.97
	Oxaliplatin	121	7.01
High and low emetogenic chemotherapy	Cyclophosphamide+methotrexate	58	3.36
Low emetogenic chemotherapy	Paclitaxel	104	6.03
	Docetaxel	34	1.97
	Gemcitabine	34	1.97
	Methotrexate	17	0.99

TABLE 8: ANTIEMETIC REGIMEN PRESCRIBED IN THE STUDY POPULATION (N=1725)

Antiemetic regimen	Number of patients	Percent
Antiemetics to treat HEC CINV: Palonosetron+dexamethasone +aprepitant	540	31.31
Palonosetron+dexamethasone	270	15.65
Antiemetics to treat both HEC and MEC CINV: Dexamethasone+palonosetron +olanzapine	190	11.01
Antiemetics to treat MEC CINV: Dexamethasone+ondansetron	518	30.03
Antiemetics to treat LEC CINV: Dexamethasone	161	9.33
Ondansetron	46	2.67

combination therapy. A combination of cisplatin plus cyclophosphamide plus dacarbazine was commonly used in the majority of patients followed by cisplatin plus dacarbazine, cyclophosphamide plus doxorubicin, and cyclophosphamide plus methotrexate. Most of the patients (n=713) were treated with HEC agent cisplatin either as monotherapy or in combination therapy. This finding is similar to those reported by Debrix *et al.*[26] and Hilarius *et al.*[27], where most of the patients were treated with HEC. However this finding is not in agreement with that reported by Baburaj *et al.*[28] and Aapro *et al.*[29], where most of the patients were treated with doxorubicin and cyclophosphamide combination, as cisplatin-induced delayed CINV intensity peaks at 2-3 d and might last for few days after the administration of chemotherapy[30]. HEC was prescribed in higher proportion in GICP group than GCCP while MEC was prescribed in higher proportion in GCCP than GICP group.

In this study, adherence to NCCN, MASCC, and ASCO guidelines were higher with GCCP group when compared to the GICP group even though these guidelines have some differences among them. All guidelines provide clinicians with updated references and a list of recommendations developed based on the international experts opinion on optimum use of antiemetics. This finding is consistent with the studies by Aapro *et al.*[29] and Gilmore *et al.*[31] proved that the guideline adherence was higher with GCCP group than GICP patients.

As the chemotherapy and antiemetics were administered using NCCN, MASCC, and ASCO guidelines the number of patients with CINV was less in the GCCP group which evident that only 46 (2.67 %) patients in GCCP had any one type of emesis, whereas 270 (15.65 %) patients in GICP group had either acute, delayed or acute and delayed emesis. Around 82 % (n=1409) have not had any episode of NV during the study period. These findings strengthen the utilization of treatment guidelines for improved QoL of cancer patients. Within the guideline groups there was no significant difference between the types of emesis, which is similar to Bloechl *et al.*[32] study where there is no difference between delayed and acute NV.

Antiemetics were considered for readministering within one-week period after the patient experience any acute or delayed emesis to control emesis and to find out the failure rate of antiemetic therapy in CINV. Among those 46 patients in GCCP and 270 patients in GICP groups with acute to acute and delayed emesis, 40 patients in GCCP and 103 patients in GICP group were observed with grade-1 NV and henceforth no antiemetics were readministered again in these patients. However, 167 patients in GICP and six patients in GCCP groups were found to have grade-2 and above NV, hence antiemetics were readministered to control the CINV, which indicate the higher failure rate (10 %) of antiemetics to control CINV. However, no iv fluids were indicated for these patients. The failure rate is more in current study GICP group (9.68 %) compared to other studies where the failure rate is very negligible as the treatment was followed using standard guidelines NCCN, MASCC and ASCO[30,32].

Among the 173 patients who fall under the category of failure of therapy, cisplatin at a dose of 70 mg/m^2, cyclophosphamide 600 mg/m^2, dacarbazine 100 mg/m^2 and doxorubicin 60 mg/m^2 produced CINV in majority of the patients. This finding is consistent with other studies that the delayed CINV is common in chemotherapy regimens that involved cisplatin, carboplatin, cyclophosphamide, and/or doxorubicin[30,33,34].

The prevalence of guideline consistent CINV prophylaxis was higher, and there were no severe CINV among patients who received antiemetics based on the guidelines when compared to those who did not receive antiemetics based on the guidelines. Similar results were observed in Gilmore *et al.*[31] study where no CINV was significantly higher in the GCCP than the GICP cohort (53.4 vs. 43.8 %). The study carried out by Aapro[29] also proved that complete response rate was higher in GCCP followers than GICP. Majority of the study participants were prescribed with palonosetron,

dexamethasone and aprepitant combination as these drugs are more effective in controlling cisplatin induced NV. In many studies, antiemetics were mostly tested on patients who received cisplatin, a HEC and most HCP agree an agent that inhibit or reduces emesis after cisplatin therapy will be effective for other chemotherapeutic agents with high-to-moderate emetogenicity[33-35].

Dexamethasone alone or in combination with 5-HT3RA and/or NK-1 receptor antagonist also recommended to alleviate CINV when patients receiving HEC/ MEC. It is extensively recommended in all guidelines that corticosteroids are the most extensively studied and are widely available. Recent studies recommend dexamethasone for the management of delayed CINV[28,30,34,35].

NV is the most common and frequently reported serious side effect of almost all anticancer agents and it adversely affect patients' daily functioning and health-related QoL. The introduction of 5HT3RA has a significant advancement in inhibiting CINV. Aprepitant, a drug which was introduced recently that selectively blocks the binding of substance-P at the NK-1 receptor in central nervous system, has been shown to have potential antiemetic activity over 5HT3RA, corticosteroid, dexamethasone, and also inhibit both acute and delayed emesis of HEC.

Clinical practice guidelines for the management of various diseases are being promoted for helping practitioners to take appropriate clinical decisions. In addition, enhance the effectiveness of drugs and reduces the health care costs. This study showed that the treatment for cancer patients was according to the standard guidelines. CINV particularly acute, delayed NV are continuing to be a significant problem for cancer patients with chemotherapy. In this study the guideline consistent group had complete response and control as less NV reported.

In the current study there were 316 patients had CINV and majority were inconsistent to the chemotherapy guidelines. However, the patients who consistent with chemotherapy guidelines have not had any emesis during and after their chemotherapy. This emphasizes the importance of following anticancer chemotherapy guidelines. Further, it proved that the patient consistent to GCCP (NCCN, ASCO and MASCC) received effective antiemetic therapy and therefore no much failure in GCCP group. However, there is 10 % failure rate in GICP group in the current practice of the tertiary care teaching hospital in India. Hence this study accentuates the strict utilization and follow up of anticancer chemotherapy guidelines.

Even though the emetogenicity of anticancer drugs are widely accepted as the most common and important risk factor for CINV, it plays a major role in the appropriate selection of antiemetic therapy. This study findings also provide support for the use of GCCP to reduce the incidence of CINV in HEC, MEC and LEC. Moreover, it also indicated that there is a major benefit of using guideline consistent antiemetic therapy to achieve CINV end points in the acute and delayed phases. Hence, this study strongly encourages the healthcare professionals of the country to adhere with all anticancer chemotherapy guidelines for better health outcomes for patients.

Acknowledgments:

Authors acknowledge the staff and management of KMCH hospital and institutions for support and encouragement to carry out this work. Author contributions: conceptualization, GK and PS; methodology, GK; software, MK; validation, NH, GK and PS; formal analysis, MK; investigation, NH; resources, GK; data curation, NH; writing, original draft preparation, GK; writing, review and editing, PS, DA and RV; visualization, MK, MA and MC; supervision, GK; project administration, NH. The authors thank the Deanship of Scientific Research at King Khalid University for providing adequate support.

Conflict of interest:

Authors declare no conflicts of interest.

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