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Assessment of Oncologist Adherence to National Comprehensive Cancer Network (NCCN) Antiemitics Guidelines for Management of Chemotherapy Induced Nausea and Vomiting in Karbala Province

Enas F. Atiyah[1*], Ayad A. Hussein[2]

[1]Faculty of Pharmacy, University of Karbalaa, Karbalaa, Iraq.
[2]Department of Clinical Pharmacy, Faculty of Pharmacy, University of Kufa, Al-Najaf, Iraq.
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Abstract

Background: Nausea and vomiting induced by chemotherapy is one of the most feared side effects of chemotherapy that affect patients' quality of life and may lead to discontinuation of chemotherapy cycles. Adherence to antiemetics guidelines such as NCCN antiemetics guidelines significantly improve the quality of treatment provided to patients while minimizing the time and money spent on each individual case.

Aim: Assessment of the current practice adherence of physicians to NCCN antiemesis guidelines.

Methods: The study is an observational cross-sectional study conducted in three oncology centers in the Iraqi province of Karbala. The study included twenty oncologists who agree to participate in the survey.

Results: Seventy percent of participants oncologists follow NCCN antiemetics guidelines, while thirty percent do not. The mean patient related risk score for Imam Al-Hussein Oncology Center, Warith International Cancer Institute, and Al-Imam Al-Hasan Al-Mujtaba Hospital was 13.5, 12.4, 14.7 respectively.

Conclusion: The current study demonstrates the knowledge and practices of participating oncologists regarding nausea and vomiting caused by chemotherapy across various oncology centers. In addition, there are a number of obstacles that make following antiemetics guidelines difficult or inconvenient, such as increased cost, a lack of awareness about antiemetics guidelines, and guidelines that are difficult or inconvenient to use.

Keywords: Adherence, NCCN guideline, cancer, chemotherapy induced nausea and vomiting, antiemetics therapy

Background

The most terrible side effects and frequent adverse events among chemotherapy patients are nausea and vomiting,[1] and may have a detrimental impact on the quality of life for cancer patients.[2] Weight loss, malnutrition, electrolyte imbalances, and dehydration, are some of the effects of CINV that might necessitate a further visit to the doctor's office, emergency room visits, or hospitalizations, necessitating the use of extra supportive care therapies. The overall cost of cancer treatment rises as a result of this increase in resource use.[3] Some studies predict that without proper preventative measures, the CINV incidence might reach as high as 70% to 90%.[4,5] A number of neurotransmitters and receptors in the central nervous system and gastrointestinal tract communicate with one another as part of the complicated multifactorial pathophysiology of CINV.[6] The central route, which predominantly affects delayed CINV,[6,7] and the peripheral pathway, which largely affects acute CINV, are the two main mechanisms that are known to effect CINV.[8,9] The principal targets of the majority of current antiemetic medicines are the neurotransmitters serotonin (5-hydroxytryptamine, or 5-HT3) and its receptor, substance P and the neurokinin-1 (NK-1) receptor, and dopamine and its receptors since they all play important roles in the activation of emesis.[10] The likelihood of developing CINV is primarily influenced by treatment-related variables, including the kind of chemotherapy, route of administration, dose of the chemotherapeutic drugs used, and timing. Patient-related risk factors should not be undervalued. These include age, sex, a history of CINV, alcohol usage, motion sickness or emesis during pregnancy, tumor load, medical issue, concurrent medications, anxiety, and dehydration.[11,12] But in actual practice, these patient-related characteristics have little impact on CINV therapy choices.[13] CINV is divided into five categories based on when nausea and illness after chemotherapy first appear: acute, delayed, breakthrough, anticipatory, and refractory.[14] When antiemetic medications are not used, chemotherapy-induced nausea and vomiting (CINV) is a common issue that affects up to 99% of patients undergoing highly emetogenic chemotherapy (HEC) and 30% to 90% of those receiving moderately emetogenic chemotherapy.[15] Neurokinin 1 (NK1) receptor antagonists, serotonin 3 (5-HT3) receptor antagonists, olanzapine, and corticosteroids (usually dexamethasone) are some of the choices for usage in CINV prevention.[16] In clinical practice, CINV is still generally undermanaged. Low adherence to antiemetic medication guidelines is one factor contributing to this.[17,18]

Methodology

Between December 2022 and January 2023, an observational cross-sectional study was conducted in three oncology centers in the Iraqi province of Karbala (Imam Al-Hussein Oncology Center, Warith International Cancer Institute, and Al-Imam Al-Hasan Al-Mujtaba Hospital). During the study period, there were a total of twenty participating oncologists from Imam Al-Hussein Oncology Center, Warith International Cancer Institute, and Al-Imam Al-Hasan Al-Mujtaba Hospital who agreed to participate in the study in order to measure their knowledge and practice in the management of CINV, as well as to evaluate the adherence to NCCN antiemetics guidelines in patients receiving chemotherapy. A validated questionnaire was used to evaluate the knowledge and practice of

oncologists in management of chemotherapy induced nausea and vomiting. This questionnaire was validated before the start of the study was conducted by experts and through performing a pilot study. Questionnaire consists of four sections: 1, 2, 3, and 4, where Section 1 examined the knowledge of the participants regarding patient-related risk factors of CINV; Section 2 involved a question about suitable anti-emetics options as recommended by the NCCN guidelines in patients receiving highly and moderately emetogenic chemotherapy; Section 3 discussed the emetogenicity of some chemotherapy drugs as classified by the NCCN guidelines; and Section 4 listed the reasons for suboptimal adherence to the anti-emesis NCCN guidelines in cancer patients.

The study was approved by the Ethical and Scientific Committee of the Faculty of Pharmacy/Kufa University (September 2022) in addition to the Scientific Committee of Research of Karbala Health Directorate (October 2022) reference number 20220169.

Statistical Analysis

Data were statistically managed and processed in two ways; Descriptive and inferential statistics. In both ways, the statistical package for social sciences (SPSS) version 28 and Microsoft Excel Program 2023 were used accordingly. Descriptive statistics of variables for oncologists and oncology patients presented as frequency and percentages for categorical (nominal or ordinal) variables and as mean, standard deviation or standard error for scale (continuous) variables. Distribution of correct responses of participant Oncologists towards Patient's-related risk factors of CINV was assessed as frequency and percentage and as a mean score which is a new variable produced by scoring the correct response with value of one while incorrect response or non-response (don't know) scored with a value of zero , this scoring based on and adopted from the scoring system reported in previous study.[19] Level of oncologists' knowledge regarding the risk factors of CINV that mentioned in guidelines was evaluated and interpreted using modified bloom's taxonomy for cognitive skills,[20] initially it was categorized into three categories based on the mean score out of one; Score <0.34: Poor, 0.34 to <0.68: Fair and 0.68–1.00: Good, for the total score out of 5: <1.67: Poor, 1.67–3.34: Fair and >3.34 Good. Comparison of frequency of barriers of adherence to guideline among oncology centers was assessed using Fisher's exact test where chi-square was inapplicable.

Results

A total of 20 oncologists were participated in the study, three oncology centers were included in the study, 9 of them from Imam Al-Hussein Oncology Center, 6 from Warith International Cancer Institute, and 5 from Al-Imam Al-Hasan Al-Mujtaba Hospital. The mean age of oncologists was 40.5 ± 4.6 years. Male oncologists were dominant, (75%). Oncologists with Board degree represented 50%, high diploma and master 45% and only one oncologist with MBChB. Among the participant oncologists, 30% had a duration in practice as oncologist of ≤ 5 years, 10 (50%) had a duration of 6–10 years and 4 (20%) had a duration in oncology practice of > 10 years. The mean duration was 8.1 ± 3.4 years (Tables 1 and 2).

Regarding following specific guideline, 14 (70%) of oncologists stated that they did, while 6 did not, 5 of the 6 oncologists who did not follow a guideline stated that they depend their clinical experience and practice while the other one oncologist stated that he followed other guidelines, (Figure 1).

When the oncologists surveyed about the patient-related risk factors of CINV that mentioned in the guidelines, their responses varied about these risk factors, however, the correct response rate ranged between 5% to 60%, giving a mean total score of 3.5 out of 9 (the number of risk factors surveyed

Table 1. **Distribution of the participant oncologists according to their centers**

Center	No.	%
Imam Al-Hussein Oncology Center	9	45.0
Warith International Cancer Institute	6	30.0
Al-Imam Al-Hasan Al-Mujtaba Hospital	5	25.0
Total	20	100.0

Table 2. **Characteristics of the participant oncologists (*N* = 20)**

Variables		No.	%
Age (year)	<40	9	45
	≥40	11	55
	Mean (SD): 40.5 (4.6)	–	–
Gender	Male	15	75
	Female	5	25
Specialty	Board/PhD	10	50
	High Diploma/Master	9	45
	MBChB	1	5
Duration in clinical practice as specialist (Years)	≤5	6	30
	6–10	10	50
	>10	4	20
	Mean (SD): 8.1 (3.4)	–	–

SD: standard deviation.

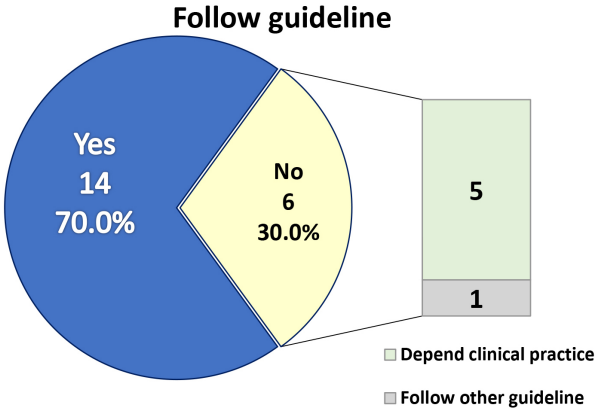

Fig. 1 **Frequency distribution of following NCCN guideline by participant oncologists (*N* = 20).**

about), which giving a level of 0.49 which was within the fair range (0.34 – 0.68), (Tables 3 and 4). Comparison of mean patient related risk score across the oncology centers revealed no significant difference across the centers in mean adherence score ($P > 0.05$), (Table 5).

Table 3. **Responses of participant Oncologists towards patient-related risk factors of CINV**

Patient-related risk factors	No.	%
Cancer patients younger than 50 years	6	30.0
Patients with history of CINV	12	60.0
Pregnancy-related nausea/vomiting	8	40.0
Female sex	4	20.0
Patient's had anxiety before chemotherapy session	10	50.0
Patient's had history of morning sickness	9	45.0
History of motion sickness	8	40.0
Patient after the 4th or more cycles of chemotherapy	12	60.0
Lower number of hours slept the night before chemotherapy	1	5.0

Table 4. **Mean scores and evaluation of responses of participant Oncologists towards patient-related risk factors of CINV**

Patient-related risk factors	Mean score out of 1	SEM	Evaluation
Cancer patients younger than 50 years	0.30	0.11	Poor
Patients with history of CINV	0.60	0.11	Fair
Pregnancy-related nausea/vomiting	0.40	0.11	Fair
Female sex	0.20	0.09	Poor
Patient's had anxiety before chemotherapy session	0.50	0.11	Fair
Patient's had history of Morning sickness	0.45	0.11	Fair
History of motion sickness	0.40	0.11	Fair
Patient after the 4th or more cycles of chemotherapy	0.60	0.11	Fair
Lower number of hours slept the night before chemotherapy	0.05	0.05	Poor
Mean total score out of 9	3.50	0.49	Fair

Evaluation: Score <0.34: Poor, 0.34 to <0.68: Fair and 0.68–1.00: Good. Total score ≤3: Poor, 3.1– 6.0: Fair and >6 Good. SEM: standard error of mean.

The responses of participant Oncologists towards the NCCN guidelines classification of emetogenic potential of intravenous antineoplastic agents, the correct response rate ranged between 50–100%, giving a good mean score level of 0.71 ± 0.05 out of one, (Tables 6 and 7).

When the oncologists asked about the possible reasons for non-adherence to the antiemesis guideline in cancer patients, majority of them (75%) attributed increased cost, lack of awareness about antiemesis guidelines (60%), need for new resources or facilities that are not available in our center (30%), non-adherence of patients (25%), unavailability of drugs (20%), guidelines are difficult or inconvenient to use in our patients (15%), concern about interaction between antiemetic agent and chemotherapy (10%), disagreement between guidelines and clinical practice and experience (10%), concern about adverse effects of antiemetic agent (5%), poor patient's compliance with treatment (5%), short duration between pre-medication and course of chemotherapy (5%) and insufficient resources reported by (5%), (Table 8). As shown in Table 9, no significant differences in the frequency of barriers of adherence to guideline among oncology centers, ($P > 0.05$).

Discussion

Most of the current study's participants are male; the mean age is 40.5, and about half have cancer scientific board certification as their primary area of expertise. Those with six to ten years of experience in the workforce made up the largest demographic. The majority of the oncologists in this study (70%) are familiar with the NCCN anti-emetics guideline; 30% are not; 25% rely on experience, practice, and judgment; and 5% use other guidelines. Better clinical results may result from following guidelines. Complete response associated to CINV was 59.9% in the group of patients which had received guideline-consistent antiemetics and 50.7% in the group not getting guideline-consistent antiemetics ($P = 0.008$) in an observational study conducted in Europe.[21] Providers can access resources from the National Comprehensive Cancer Network (NCCN) to enhance the quality and efficiency of cancer care for oncology patients.[22] The NCCN anti-emesis guidelines are widely used by clinicians in community oncology places because they provide an overview of treatment to avoid CINV in patients receiving chemotherapy.[23]

In this study, oncologists' replies differed when asked about the patient-related risk factors of CINV specified in the guidelines. Some patient-related risk factors, including being less than 50 years old, being female, and getting less than six hours of sleep the night before chemotherapy, were poorly evaluated by the participating oncologists (mean score 0.3, 0.2,

Table 5. **Comparison of mean patient related risk score across the oncology centers**

	Risk score				*P* value*
	No.	Mean	SE	95% CI	
Imam Al-Hussein Oncology Center	60	13.5	0.6	12.3–14.8	0.071 NS
Al-Imam Al-Hasan Al-Mujtaba Hospital	64	12.4	0.5	11.5–13.4	
Warith International Cancer Institute	50	14.7	0.8	13.2–16.3	
Total	174	13.5	0.4	12.8–14.2	

SE: standard error of mean, 95% Confidence Interval for Mean, NS: not significant. * Kruskal-Wallis H test was applied.

Table 6. **Responses of participant Oncologists towards the NCCN guidelines classification of emetogenic potential of intravenous antineoplastic agents**

Chemotherapy agent	Correct		Incorrect	
	No.	%	No.	%
Anthracycline-cyclophosphamide	19	95.0	1	5.0
Cisplatin	20	100.0	0	0.0
Dacarbazine	10	50.0	10	50.0
Busulfan	11	55.0	9	45.0
Clofarabine	11	55.0	9	45.0

Table 7. **Mean scores and evaluation of responses of participant Oncologists towards the NCCN guidelines classification of emetogenic potential of intravenous antineoplastic agents**

Chemotherapy agent	Mean score out of 1	SEM	Evaluation
Anthracycline-cyclophosphamide	0.95	0.05	Good
Cisplatin	1.00	0.00	Good
Dacarbazine	0.50	0.11	Fair
Busulfan	0.55	0.11	Fair
Clofarabine	0.55	0.11	Fair
CINV Total risk score (out of 5)	3.55	0.26	Good
CINV Mean risk score of 1	0.71	0.05	Good

Evaluation: Score <0.34: Poor, 0.34 to <0.68: Fair and 0.68–1.00: Good. Total score <1.67: Poor, 1.67–3.34: Fair and >3.34 Good. SEM: standard error of mean.

Table 8. **Reasons/barriers for under-use or suboptimal adherence to the antiemesis guideline in cancer patients according to the Oncologists' opinion**

Reason*	No.	%
Increased cost	15	75.0
Lack of awareness about antiemesis guidelines	12	60.0
Need for new resources or facilities that are not available in our center	6	30.0
Non-adherence of patients	5	25.0
Unavailability of drugs	4	20.0
Guidelines are difficult or inconvenient to use in our patients	3	15.0
Disagreement between guidelines and clinical practice and experience	2	10.0
Concern about interaction between antiemetic agent and chemotherapy	2	10.0
Concern about adverse effects of antiemetic agent	1	5.0
Poor patient's compliance with treatment	1	5.0
Short duration between pre-medication and course of chemotherapy	1	5.0
Insufficiency of resources	1	5.0

*Some oncologists mentioned more than one reason.

and 0.05, respectively). Other patient-related risk factors such as patients with a history of chemotherapy-induced nausea and vomiting (CINV), nausea and vomiting during pregnancy, anxiety before chemotherapy sessions, a history of morning sickness, or a history of motion sickness were all evaluated fairly by participating oncologists, with mean scores of 0.6, 0.4, 0.5, 0.45, and 0.6. Imam Al-Hussein Oncology Center had a mean risk score of 13.5, Al-Imam Al-Hassan Al-Mujtaba Hospital had a mean risk score of 12.4, and Warith International Cancer Institute had a mean risk score of 14.7 ($P = 0.071$). In contrast to our results, eight risk factors for chemotherapy-induced nausea and vomiting (CINV) were identified in a study by Dranitsaris et al.[24] These factors included anticipatory nausea and vomiting, age <60 years, the use of platinum or anthracycline-based chemotherapy regimens, history of nausea and vomiting, less than seven hours of sleep the night before chemotherapy, CINV in a previous cycle, less than seven hours of sleep the night before chemotherapy, patient self-medication with non-prescribed treatment, and the first two cycles of chemotherapy.[24]

Based on the NCCN recommendations, our findings demonstrated a good mean score level of 0.71 ± 0.05 out of one for the classification of intravenous antineoplastic drugs' emetogenic potential.

We have documented numerous obstacles that impact the adherence of oncologists to the NCCN guidelines for antiemetics. Among these barriers, the most prominent one, accounting for 75% of the total, is the increase in cost. The financial burden associated with medicine might potentially hinder a patient's access to and use of efficacious antiemetic treatment. When patients are unable to pay the full cost of their prescribed medications, they may perceive prophylaxis as being of lesser importance until they experience the real manifestation of the problem. Up to 32% of older persons take less medicine than is recommended to save money.[25]

Other challenges include a lack of awareness about antiemesis guidelines, which accounts for 60% of the problem. Low levels of guideline awareness may be attributable to a lack of continuing education among health care providers.[26] The widespread distribution of educational resources, however, may not be enough. Prophylactic treatment advised by recommendations was much more likely to be used when guidelines were disseminated in conjunction with an "audit-and-feedback" technique and an educational outreach visit, according to a study of 103 Italian cancer centers.[27]

Thirty percent of the barriers are related to the need for new resources or facilities that are not available at our center. The introduction of protocols at the institutional level has the potential to enhance staff comprehension regarding the range of antiemetic medications accessible to patients.[28] Adherence to antiemetic therapy guidelines was observed to improve in a U.S. hospital after the installation of a program that includes an educational session, risk-assessment tools, and computerized standard order sets.[29]

Non-adherence of patients accounts for 25%. In a distinct survey encompassing physicians, oncology nurses, and patients, it was observed that a slightly greater percentage of patients (38%) expressed non-compliance with their prescribed antiemetic regimen at home. The patients cited their hesitation to consume medication until experiencing symptoms and their apprehension that ingesting an oral tablet might trigger nausea and/or vomiting.[30]

Table 9. **Comparison of frequency of barriers of adherence to guideline among oncology centers**

Stated barrier	Center						*P* value*
	Oncology center		Immam Hasan Hospital		Warith International Cancer Institute		
	No.	%	No.	%	No.	%	
Lack of awareness about antiemesis guidelines	5	25.0	2	10.0	5	25.0	0.442 ns
Concern about adverse effects of antiemetic agent	1	5.0	0	0.0	0	0.0	NA
Concern about interaction between antiemetic agent and chemotherapy	2	10.0	0	0.0	0	0.0	NA
Guidelines are difficult or inconvenient to use in our patients	1	5.0	1	5.0	1	5.0	1.00 ns
Need for new resources or facilities that are not available in our center	3	15.0	2	10.0	1	5.0	0.698 ns
Disagreement between guidelines and clinical practice and experience	2	10.0	0	0.0	0	0.0	0.479 ns
Increased costs	8	40.0	3	15.0	4	20.0	0.524 ns
Non-adherence of patients	3	15.0	0	0.0	2	10.0	0.437 ns
Unavailability of drugs	3	15.0	1	5.0	0	0.0	0.311 ns
Others**	0	0.0	1	5.0	2	10.0	0.145 ns

*Fisher's exact test used in all comparisons. **Deficiency of resources, Poor patient compliance with treatment, short duration between pre-medication and course of chemotherapy, patient awareness especially in delayed phase. NA: not applicable, ns: not significant.

Unavailability of drugs constitutes 20%. The availability of medications like aprepitant, which has been shown to be particularly effective in the prevention of nausea and vomiting, was one of the practical obstacles that prevented the guidelines from being applied despite their implementation. After severely emetogenic treatment, which may include medications such as cisplatin, such drugs are need to be taken.[31]

Guidelines are difficult or inconvenient to use for our patients, and disagreements between guidelines and clinical practice and experience account for 15% and 10%, respectively. Cabana et al. have categorized obstacles to physician adherence to clinical practice guidelines into three different groups. These groups are knowledge barriers, which encompass a lack of awareness and familiarity with the guideline; attitude barriers, which involve disagreement with evidence-based medicine and specific guidelines, as well as a lack of belief in the efficacy of guidelines and the ability to comply with their recommendations; and behavior barriers, which encompass patient preferences and characteristics of practice relating to the guidelines.[32]

Furthermore, approximately 10% of barriers are attributed to concern about interaction between antiemetic agent and chemotherapy. Regardless of the kind, drug interactions have the potential to seriously impair the effectiveness of treatment or raise drug toxicity, with potentially fatal clinical outcomes. There have been several reports of drug interactions between chemotherapy, antineoplastic therapy, supportive therapy, and other commonly used medications in clinical practice.[33,34]

Concern about adverse effects of antiemetic agent accounts for 5% of the obstacles. This is in line with the results of a survey of oncology professionals in the United Kingdom, which found that various adverse effects were associated with antiemetic usage for the management of CINV. One of the most common was constipation as a result of therapy with 5HT3 receptor antagonists.[35]

Conclusion

The current study demonstrates the knowledge and practices of participating oncologists regarding nausea and vomiting caused by chemotherapy across various oncology centers. In addition, there are a number of obstacles that make following antiemetics guidelines difficult or inconvenient, such as increased cost, a lack of awareness about antiemetics guidelines, and guidelines that are difficult or inconvenient to use.

Recommendation

Further research is necessary to investigate the extent of knowledge regarding chemotherapy-induced nausea and vomiting (CINV) and adherence to prophylaxis guidelines. This should involve bigger sample sizes and the inclusion of multiple medical centers.

Training workshops are often conducted for health workers with the aim of preventing chemotherapy-induced nausea and vomiting (CINV).

Competing Interests

According to the authors, no conflicts of interest exist.

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