Guideline Adherence Matters: Rates and Consequences of Non-Adherence to Antiemetic Practice Guidelines

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BACKGROUND

➢Chemotherapy-induced nausea and vomiting (CINV) is one of the most common, yet most debilitating, side effects of cancer treatment, associated with poor quality of life and impacting treatment completion.

➢Several antiemetics, including the 5-HT3 receptor antagonists and the more recent NK-1 receptor antagonists such as aprepitant, have significantly improved the control of CINV, thereby improving the rates of adherence to potentially curative treatment, and the health-related quality of life.

➢Adherence to antiemetic guidelines from professional societies (MASCC, ESMO, ASCO) can prevent up to 70-80% of CINV. Few quality control studies have assessed the actual adherence rates and the associated efficacy of the practice guidelines, especially in Canada.

➢The literature currently reports adherence rates from 10% to 99%, further emphasizing the variability across the world.

OBJECTIVES

➢Evaluate the proportion of patients treated with highly (HEC) or moderately emetogenic chemotherapy (MEC) who received antiemetic regimens adherent to the MASCC 2010 Antiemetic practice guideline at the Nova Scotia Cancer Center (NSCC) in Halifax, Canada.

➢Assess the rates of chemotherapy-induced nausea and vomiting (CINV) in our population at the NSCC in Canada.

METHODS

➢A provincial retrospective chart review was performed on all adult patients (n=262) with a solid malignancy at any stage who received their first cycle of HEC (including AC regimen) or MEC at the NSCC between February-July 2016 inclusively.

➢Patients were excluded if they received a low-emetogenic chemotherapy regimen, if they had received any other chemotherapy within one year prior to inclusion in the study, or if their toxicity assessment was incomplete or absent. Patients who had prior radiation or surgery were included.

➢Rate of adherence to the 2010 MASCC/ESMO Antiemetic Guidelines and rates of CINV based on the 2009 Common Toxicity Criteria vers. 4 were analyzed.

➢We classified grade 0 nausea and vomiting as complete control, grade 1-2 nausea and vomiting as partial control, and grade 3+ nausea and vomiting as poor control.

➢Statistical analysis was performed using Students t-test, Fisher exact test, and Chi-Square test.

MASCC 2010 Antiemetic Guideline

Nausea and Vomiting	Acute			Delayed	
EMETIC RISK GROUP	ANTIEMETICS (D1)			ANTIEMETICS (D2-D3)	
High	5HT3	+ DEX	+ APR	DEX	APR
Anthracycline + Cyclophosphamide (AC)	5HT3	+ DEX	+ APR	APR	
Non-AC Moderate	5HT3	+ DEX		DEX	
Low	DEX	or 5HT3	or DRA	No routine prophylaxis	

5HT3 = serotonin$_3$ receptor antagonist; DEX = DEXAMETHASONE; APR = APREPITANT; DRA = Dopamine receptor antagonist

Acute: first 24 hours
Delayed: Day 2 and 3

*AC combinations are considered a special case of MEC that should be managed with a NK-1 antagonist like HEC in the MASCC 2010 guidelines, but in 2016 it is considered HEC (Aprepitant is recommended for prophylaxis in both guidelines).

RESULTS

DEMOGRAPHICS

	AD (n=168)	NA (n=94)	p
Sex			
Female	126 (75%)	60 (64%)	0.06
Male	42 (25%)	34 (36%)	
Age			
Range	34-86	19-89	
Median	65	58	
Average	64.1	57.1	<0.001
Cancer Type			
Breast	25 (14.9%)	42 (44.7%)	<0.0001
Lung	29 (17.3%)	22 (23.4%)	0.256
Colorectal	27 (16.1%)	5 (5.3%)	0.01
Ovarian	53 (31.5%)	2 (2.1%)	<0.0001
Uterine	21 (12.5%)	4 (4.3%)	0.03
Head and neck	4 (2.4%)	8 (8.5%)	0.031
Bladder	2 (1.2%)	3 (3.2%)	0.351
Esophagus	3 (1.8%)	2 (2.1%)	1
Pancreaticobiliary	1 (0.6%)	1 (1.1%)	1
Other*	2 (1.2%)	6 (6.4%)	0.01
Stage			
1	23 (13.7%)	6 (6.4%)	
2	17 (10.1%)	19 (20.2%)	0.01
3	65 (38.7%)	46 (48.9%)	0.107
4	54 (32.1%)	25 (26.6%)	0.268
ECOG			
0	85 (50.6%)	60 (63.8)	
1	63 (37.5%)	28 (29.8%)	0.128
2	16 (9.5%)	5 (5.3%)	0.154
>2	3 (1.8%)	0 (0%)	0.272
Comorbidities			
Cardiac	20 (11.9%)	11 (11.7%)	1.0
Respiratory	23 (13.7%)	17 (18.1%)	0.373
Diabetes	25 (14.9%)	7 (7.4%)	0.114
Other malignancies	32 (19.0%)	11 (11.7%)	0.164
Drug plan			
Yes	110 (65.5%)	65 (69.1%)	0.49
No	12 (7.1%)	10 (10.6%)	
Unknown	46 (27.4%)	19 (20.2%)	
Prior Radiation			
Yes	33 (19.6%)	25 (26.6%)	0.216
No	135 (80.4%)	69 (73.4%)	
Prior Surgery			
Yes	101 (60.1%)	52 (55.3%)	0.514
No	67 (39.9%)	42 (44.7)	

CHEMOTHERAPY

	AD (n=168)	NA (n=94)	p
Chemo emetogenicity			
HEC (+AC)	7 (4.2%)	73 (77.7%)	<0.0001
MEC	161 (95.8%)	21 (22.3%)	
Chemo regimen			
Cisplatin	7 (4.2%)	35 (37.2%)	<0.0001
FEC/AC	0 (0%)	38 (40.4%)	<0.0001
Carboplatin	108 (64.2%)	11 (11.7%)	<0.0001
TC	25 (14.9%)	4 (4.2%)	0.007
Oxali/Irinotecan	28 (16.7%)	6 (6.4%)	0.02
Dose reduction			
Yes	39 (23.2%)	17 (18.1%)	0.351
No	129 (76.8%)	77 (81.9%)	

TOXICITY & ANTI-EMETIC

	AD (n=168)	NA (n=94)
Toxicity Grade		
Nausea		
0	103 (61.3%)	50 (53.2%)
1	52 (30.9%)	36 (38.3%)
2	13 (7.7%)	5 (5.3%)
3	0 (0%)	3 (3.1%)
Vomiting		
0	147 (87.5%)	75 (79.8%)
1	14 (8.3%)	10 (10.6%)
2	5 (3.0%)	6 (6.4%)
3	2 (1.2%)	1 (1.1%)
4	0 (0%)	2 (2.1%)
Breakthrough Rx		
Metoclopramide	121 (72%)	50 (53.2%)
Prochlorperazine	45 (26.8%)	41 (43.6%)
Ondansetron	4 (2.4%)	9 (9.6%)
Dimenhydrinate	1 (0.6%)	1 (1.1%)

CAUSES OF NON-ADHERENCE

Drug	83 (88%)
Duration	17 (18%)
Dose	6 (6%)
Frequency	5 (5%)
No breakthrough Rx	3 (4%)

➢80 (30.5%) patients received HEC, including AC regimens (FEC and AC), and 182 (69.5%) received MEC.

➢Adherence Rate to the 2010 MASCC Antiemetic guideline in our patient population was **64.1%.**

➢Among the 94 cases of non-adherence, 73 received a HEC regimen, consistent with a **significantly higher rate of non-adherence with HEC as opposed to MEC (p<0.01)**.

➢Rate of nausea and vomiting (grade 1+) in the entire population was **41.6%**. There was higher rate of nausea and vomiting in non-adherent group compared to adherent group, although not statistically significant (p=0.2). There was a statistically significant higher rate of partially and poorly controlled nausea with vomiting (v1+) in the non-adherent HEC group when compared to the rest of the adherent group (p=0.03).

➢Non-adherence was most commonly due to inadequate antiemetic combinations, specifically the **omission of a NK1 antagonist for HEC**. In our study 100% of AC regimens (FEC-D, FEC-100, AC) did not receive a NK-1 antagonist, and majority of cisplatin containing regimens also omitted aprepitant. This is likely due to the fact that pre-printed chemotherapy order forms did not have aprepitant as an option for AC regimens.

➢Carboplatin is considered MEC in both 2010 and 2016 but as of 2016, it is recommended to use NK-1 antagonist for prevention of acute nausea and vomiting in carboplatin-containing regimen. In this study, carboplatin was the most commonly used MEC chemotherapy (n=119): NK-1 antagonist was not required for adherence nor was it prescribed for any patient. Rates of combined nausea and vomiting (N/V1+) in carboplatin containing regimens were 35.5%.

CONCLUSIONS

➢Adherence rate to 2010 MASCC antiemetic guideline at the NSCC in 2016 was 64.1%, comparable to what the literature reports.

➢Patients receiving HEC had higher rate of non-adherence, and non-adherent patients on HEC experienced higher rate of nausea with vomiting.

➢This study illustrates the importance of adherence to antiemetic guidelines for prevention of CINV. Strategies to improve adherence rate may include:

➢Implement changes to pre-printed chemotherapy order forms to include NK-1 antagonist (aprepitant) for cisplatin-based chemotherapy, as well as AC combination regimens.

➢Reassess system access level for provincial and private drug coverage.

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