

Chemotherapy-Induced Nausea and Vomiting in Breast Cancer Patients: A Multicenter Prospective Observational Study

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ABSTRACT

Objective: This study aimed to assess the occurrence of chemotherapy-induced nausea and vomiting (CINV) in acute phase (24 h after chemotherapy) and delayed phase (2–5 days after chemotherapy) after standard antiemetic therapy and to explore the risk factors of CINV in the acute and delayed phases.

Methods: This prospective and observational study analyzed the data of 400 breast cancer patients scheduled for chemotherapy in two hospitals. The self-report survey was developed to assess the occurrence of CINV and their associated factors. On day 2 and day 6 of chemotherapy, CINV was evaluated by the Multinational Association of Supportive Care in Cancer Antiemetic Tool (MAT). The incidence of acute and delayed CINV was expressed as frequency and percentage. **Results:** Among

400 patients, 29.8% and 23.5% experienced acute and delayed CINV, respectively. Logistic regression analysis showed that the risk factors associated with acute CINV included pain/insomnia, history of CINV, and highly emetogenic chemotherapy. The history of motion sickness (MS), history of CINV, number of chemotherapy cycles completed, and the incidence of acute CINV were significant risk factors for delayed CINV (all $P < 0.05$).

Conclusions: The results of this study are helpful for nurses to identify high-risk patients with CINV, formulate effective treatment plans, and reduce the incidence of CINV.

Key words: Antiemetic guidelines, breast cancer, chemotherapy-induced nausea and vomiting, risk factors

Introduction

Breast cancer is a global public health problem.^[1] Chemotherapy is one of the primary treatments of breast cancer, but a series of adverse reactions, such

as chemotherapy-induced nausea and vomiting (CINV), are still inevitable.^[2,3] Clinically, the most common types are acute and delayed CINV. Acute CINV usually occurs

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within a few minutes to several hours after administration and commonly resolves within the first 24 h. Delayed CINV occurs more than 24 h after chemotherapy and can last for 6–7 days.^[4]

Studies have shown that in the chemotherapy regimens used by breast cancer patients, the incidence of CINV is as high as 60%–90%,^[5] especially late-onset nausea and vomiting, which is most difficult to control and accurately predict.^[6,7] Not only can CINV lead to such problems as electrolyte disorder and malnutrition, but also it can increase the patient’s anxiety, depression, and other negative emotions, reduce the patients’ adherence to treatment, and even lead to interruption of treatment, life-threatening.^[8-11] Besides, CINV also causes medical resource burden.^[12,13] Therefore, identifying its risk factors is crucial for effective symptom management.

The purpose of this study was to examine the incidence and factors associated with acute and delayed CINV among Chinese breast cancer patients.

Methods

Study design and patients

The study adopted a prospective cohort design. Potential individuals were recruited from inpatient wards of two hospitals in Hunan province of China during the period November 2019 to July 2020. Eligible criteria were Chinese women who were over 18 years old, diagnosed with breast cancer, and scheduled to receive chemotherapy during the data collection period. Those who had cognitive or communication disorders, were participating in other related researches during the study period, and had other conditions that may cause nausea or vomiting (e.g., intestinal obstruction and pregnancy) were excluded from the study.

Measurements

According to the CINV assessment tool of Multinational Association of Supportive Care in Cancer (MASCC),^[14] the acute CINV was defined as cumulative number of vomiting episodes within 24 h ≥ 1 or nausea level >3 , and the definition of delayed CINV was cumulative number of vomiting episodes within 2–6 days ≥ 1 or nausea >3 . In this study, the occurrence of CINV was defined as over the past 24 h (acute CINV) and 2-5 days (delayed CINV) following the completion of chemotherapy.

Based on extensive literature reading,^[15] combined with clinical practice and group discussion, a list of 26 CINV-related factors were identified [Table 1]. The Chinese version of MASCC Antiemetic Tool (MAT)^[16] was used to identify the occurrence of acute and delayed CINV, and the

Table 1: Patients’ characteristics (n=400)

Variable	Category	n (%)
Age (years)	<40	51 (12.8)
	40-60	297 (74.3)
	≥ 60	72 (13.0)
Marital status	Married	382 (95.5)
	Other	18 (4.5)
Education	Primary school and below	152 (38.0)
	Junior high school	164 (41.0)
	High school or technical secondary school	40 (10.0)
	Junior college and above	44 (11.0)
BMI	<18.5	13 (3.3)
	18.5-23.9	219 (54.7)
	24-27.9	136 (34.0)
	≥ 28	32 (8.0)
Work status	Yes	35 (8.8)
	No	365 (91.2)
Alcohol consumption	Yes	17 (4.3)
	No	383 (95.7)
Smoking	Yes	7 (1.8)
	No	393 (98.2)
CINV history	Yes	152 (38.0)
	No	248 (62.0)
PS	≤ 1	326 (81.6)
	≥ 2	74 (18.4)
Sleep <7 h before chemotherapy	Yes	189 (47.3)
	No	211 (52.8)
History of MS	Yes	191 (52.3)
	No	209 (47.7)
History of vomiting during pregnancy	Yes	179 (44.8)
	No	221 (55.2)
Pain/insomnia	Yes	226 (56.5)
	No	174 (43.5)
Constipation	Yes	124 (31.0)
	No	276 (69.0)
Over-the-counter home medicines	Yes	19 (4.8)
	No	381 (95.2)
Prechemotherapy anxiety	Yes	109 (27.3)
	No	291 (72.7)
Diabetes	Yes	25 (6.3)
	No	375 (93.7)
Hypertension	Yes	52 (13.0)
	No	348 (87.0)
Chronic renal insufficiency	Yes	2 (0.5)
	No	398 (99.5)
Coronary heart disease	Yes	10 (2.5)
	No	390 (97.5)
Metastasis	Yes	208 (52.0)
	No	192 (48.0)
Pathological pattern	Invasive nonspecific carcinoma	358 (89.5)
	Other	42 (10.5)
Disease stage	1	61 (15.2)
	2	190 (47.5)
	3	111 (27.8)
	4	38 (9.5)

Contd...

Table 1: Contd...

Variable	Category	n (%)
Chemotherapy regimen	Low	105 (26.3)
	Moderate	80 (20.0)
	High	215 (53.7)
Chemotherapy cycle number (cycles)	<3	211 (52.8)
	≥3	189 (47.2)
Antiemetic	Single	127 (31.8)
	Double	154 (38.5)
	Triple	119 (29.7)

Chemotherapy regimens: Low: navelbine, TAX (Taxol), Xeloda, gemcitabine, docetaxel; Moderate: cyclophosphamide + doxorubicin; High: Cisplatin, Pharmorubicin; marital status: Other (those who are never married, divorced, or widowed). BMI: Body mass index, CINV: Chemotherapy-induced nausea and vomiting, MS: Motion sickness, PS: Performance Status

Chinese version of Generalized Anxiety Disorder Scale-7 was adopted to assess the severity of anxiety.^[17]

Data collection and ethical consideration

This study was approved by the Ethics Committee of Hunan Cancer Hospital (Approval No. 2019-21). A research nurse recruited eligible individuals on the 1st day admitted to the ward. Written informed consent was obtained from those who were willing to participate in the study.

All the consented participants were invited to have a face-to-face interview during the second day of chemotherapy to collect acute CINV data. A followed up telephone interview was conducted on the 6th day after chemotherapy to collect delayed CINV data.

Statistical analysis

All statistical analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Demographic data of patients and the incidence of acute and delayed CINV were presented by frequency and percentage. Univariate analyses were conducted on the 26 factors listed in Table 1 to identify potential risk factors for each type of CINV. Factors with $P < 0.10$ in univariate analysis were selected as candidate independent variables in a backward multivariable logistic regression analysis to delineate significant risk factors for each type of CINV. All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

Results

A total of 420 subjects were recruited, 20 patients were later excluded from the analysis because of incomplete data [Figure 1]. The background characteristics of the participants are presented in Table 1. The incidence rates of acute and delayed CINV were 29.8% ($n = 400$) and 23.5% ($n = 400$), respectively.

The multivariate logistic regression analysis revealed that pain/insomnia (odds ratio [OR] = 1.9, 95% confidence interval [CI]: 1.1–3.1, $P = 0.016$), history of CINV (OR = 4.0, 95% CI: 2.0–6.6, $P < 0.001$), and high

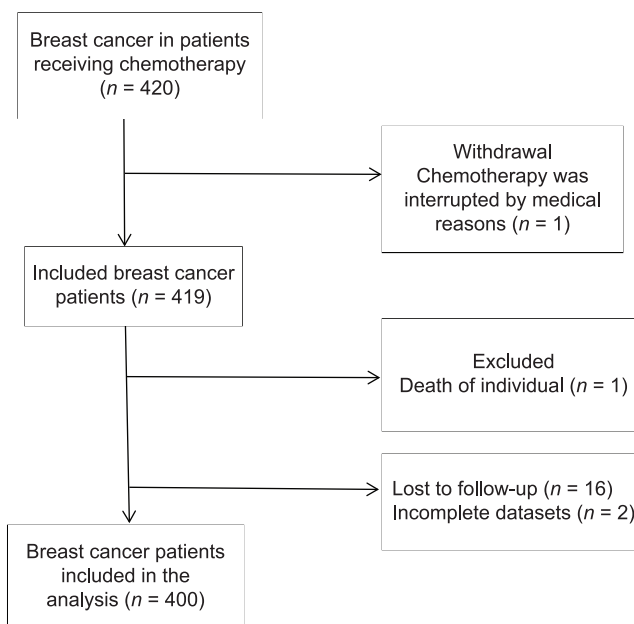


Figure 1: Patients' flowchart

emetic chemotherapy regimen (OR = 4.5, 95% CI: 2.3–8.5, $P < 0.001$) were significantly associated with an increased odds for an occurrence of CINV in acute phases [Table 2].

History of CINV (OR = 2.8, 95% CI: 1.6–5.0, $P < 0.001$), history of MS (OR = 1.7, 95% CI: 1.0–2.7, $P = 0.045$), and acute CINV occurred (OR = 2.6, 95% CI: 1.6–4.4, $P < 0.001$) were associated with an increased odds of delayed CINV. In contrast, the number of chemotherapy cycles completed was significantly associated with a decreased risk for CINV in delayed phase (OR = 0.5, 95% CI: 0.3–0.9, $P = 0.031$). The risk of CINV was higher in the first two chemotherapy cycle numbers than in subsequent rounds of chemotherapy [Table 3].

Discussion

The findings of the study highlight a considerable proportion of participants suffered from CINV and the associations of CINV with treatment and patient-related factors.

It is worth noting that in our study, CINV in the acute stage is even slightly higher than that in the delayed stage. It may be related to adequate antiemetic prophylaxis. Moreover, the discharged patient received dietary guidance and psychological comfort from nurses. This may be also helpful to control CINV in the delayed phase.

This study identified pain/insomnia, history of CINV, high emetic chemotherapy regimens are associated with an increased risk of acute CINV; these results are consistent with those reported in previous studies.^[18-20] Pain/insomnia may aggravate the physical burden of patients, make their physical strength decline, reduce the ability to deal with adverse reactions, and may

Table 2: Univariate and multivariable logistic regression to identify factors associated with acute chemoradiation-induced nausea and vomiting

Variable	Category	Univariate analysis		Multivariable analysis	
		OR (95% CI)	P	OR (95% CI)	P
Education	Primary school and below (ref)		0.300	NR	
	Junior high school	0.6 (0.3-1.0)	0.062		
	High school or technical secondary school	0.6 (0.2-1.6)	0.320		
	Junior college and above	0.7 (0.3-1.9)	0.532		
Pain/insomnia		2.0 (1.1-3.6)	0.016	1.9 (1.1-3.1)	0.016
Diabetes		3.6 (1.2-11.3)	0.026	NR	
Prechemotherapy anxiety		1.9 (1.1-3.4)	0.025	1.7 (1.0-2.8)	0.054
History of CINV		5.6 (2.7-10.9)	<0.001	4.0 (2.0-6.6)	<0.001
BMI	< 18.5 (ref)		0.217	NR	
	18.5-23.9	9.2 (1.0-86.7)	0.050		
	24-27.9	8.1 (0.8-77.9)	0.070		
	≥28	5.2 (0.4-67.7)	0.204		
Chemotherapy regimens	Low (ref)		<0.001		<0.001
	Moderate	2.2 (0.8-6.0)	0.122	1.8 (0.8-4.2)	0.181
	High	6.9 (2.7-13.3)	<0.001	4.5 (2.3-8.5)	<0.001

Only those factors with $P < 0.1$ in univariate analyses are listed in the table. Ref: Reference category, NR: Not retained in backward multivariable logistic regression, CI: Confidence interval, CINV: Chemoradiation-induced nausea and vomiting, OR: Odds ratio, BMI: Body mass index

Table 3: Univariate and multivariate logistic regression to identify risk factors for delayed chemotherapy-induced nausea and vomiting

Variable	Univariate analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
History of MS	1.7 (1.0-3.0)	0.069	1.7 (1.0-2.7)	0.045
History of CINV	3.3 (1.7-6.5)	<0.001	2.8 (1.6-5.0)	<0.001
Chemotherapy cycle number	0.4 (0.2-0.8)	0.013	0.5 (0.3-0.9)	0.031
Acute CINV occurred	3.0 (1.7-5.5)	<0.001	2.6 (1.6-4.4)	<0.001

Only those factors with $P < 0.1$ in univariate analyses are listed in the table. CI: Confidence interval; CINV: Chemotherapy-induced nausea and vomiting, MS: Motion sickness, OR: Odds ratio

result in experiencing CINV. This suggests that more attention should be paid to the management of CINV for patients with symptoms such as pain and insomnia before chemotherapy. Previous history of nausea and vomiting is another factor of acute CINV. It may be due to nausea and vomiting are usually caused by conditioned stimuli, patients with a prior history of CINV are at higher risk of nausea and vomiting when exposed to the same stimuli. The emetic potential of drugs has long been recognized as an important factor influencing CINV. Although preventive treatment was provided in strict accordance with the guidelines during chemotherapy, the risk of acute CINV is still high. The treatment for this group of patients needs to be further improved.

Four influencing factors of delayed CINV were identified: history of MS, history of CINV, number of chemotherapy cycles completed, and acute CINV. Although patients with acute CINV received a higher dosage of antiemetic drugs, they still experience delayed CINV, indicating that individual factors determine who is more susceptible to CINV or unresponsive to antiemetic drugs, in particular

those with history of CINV or MS. The findings of the study may be useful for nurses to identify the high-risk group of delayed CINV and provide timely education of symptom assessment and management to them. The risk after three or more cycles of chemotherapy is only 0.5 times that following the first two cycles. The possible reason may be due to patients who have experienced chemotherapy gradually acclimate to the drug and endure the adverse reactions in later cycles, the experience of nausea and vomiting is not obvious.

Conclusions

The findings of the study highlight a considerable proportion of participants suffered CINV though the occurrence rate of CINV was lower than previous studies. This study is the first report to demonstrate that, among patients with breast cancer chemotherapy treatment, those having a pain/insomnia and chemotherapy cycle number <3 represent high-risk populations, whereas those who occur with CINV in the acute phase increase the risk of CINV in the delayed phase. The findings may help nurses working for Chinese population in identifying patients at risk for CINV and in planning effective symptom management.

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Conflicts of interest

There are no conflicts of interest.

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