# Incidence and management of chemotherapy-induced nausea and vomiting in women with breast cancer



Ocorrência e manejo de náusea e vômito no tratamento quimioterápico em mulheres com câncer de mama

Incidencia y gestión de náuseas y vómitos en tratamiento quimioterapico en mujeres con cáncer de mama

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#### **ABSTRACT**

The objective of this study was to analyze the incidence of chemotherapy-induced nausea and vomiting in women with breast cancer and identify strategies used by them to control these signs and symptoms. Data for this cross-sectional study were collected through interviews during the last cycle of chemotherapy, between August 2011 and March 2012, in a university hospital in the State of São Paulo. The sample consisted of 22 women between the ages of 31 and 70, of whom 77.3% reported nausea and 50% vomiting during treatment. Regarding symptom management, 82% of the women reported having received some information centered on the use of prescribed medication. However, 27.3% did not know what medication they had taken. We concluded that there is a lack of systematic care and institutional protocol to guide professionals in providing standardized information to women so they can better control nausea and vomiting.

**Descriptors:** Toxicity. Chemotherapy. Nausea. Vomiting. Nursing.

#### **RESUMO**

Objetivou-se analisar a ocorrência de náusea e vômito em mulheres com câncer de mama durante a quimioterapia, e identificar o manejo utilizado para o controle desses sinais e sintomas. Pesquisa transversal, cujos dados foram coletados por meio de entrevista, no último ciclo de quimioterapia, entre agosto de 2011 e março de 2012 em um hospital universitário no interior do Estado de São Paulo. A amostra foi composta por 22 mulheres, com idade entre 31 e 70 anos, e 77,3% relataram náusea e 50% vômito, durante o tratamento. Quanto ao manejo, 82% delas afirmaram ter recebido algum tipo de informação que ficou centrada no uso da medicamento prescrito, entretanto, 27,3% não souberam responder qual medicamento usaram. Concluiu-se que há falta de sistematização da assistência e protocolo institucional que norteiem os profissionais a fornecer informações padronizadas, possibilitando o seguimento das mulheres, a fim de terem controle mais adequado da náusea e vômito.

**Descritores:** Toxicidade. Quimioterapia. Náusea. Vômito. Enfermagem.

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# RESUMEN

Este estudio objetivó analizar la incidencia de náuseas y vómitos en mujeres con cáncer de mama durante la quimioterapia, identificar el manejo utilizado para controlar estos signos y síntomas. Estudio transversal, cuyos datos fueron recolectados por medio de entrevistas en el último ciclo de quimioterapia entre agosto 2011 y marzo 2012 en un hospital universitario en el Estado de São Paulo. La muestra consistió de 22 mujeres, con edades entre 31 y 70 años, que el 77,3% reportó náuseas y el 50% vómitos durante el tratamiento. Cuanto al manejo, el 82% afirmó que habían recibido algún tipo de información centrada en el uso de la medicación prescrita, sin embargo, el 27,3% no supo responder cuál medicación fue utilizada. Se concluye que falta de sistematización de la atención y protocolo institucional para orientar profesionales para ofrecer información estandarizada, posibilitando el seguimiento de las mujeres para tener un mejor control de náuseas y vómitos.

Descriptores: Toxicidad. Quimioterapia. Náusea. Vómitos. Enfermería.

## **■ INTRODUCTION**

Nausea and vomiting are the most stressful and uncomfortable symptoms reported by oncology patients. Approximately half of all cancer patients will experience nausea and vomiting during some phase of the disease. Studies indicate a variation of 38% to 60% prevalence of these symptoms during chemotherapy.<sup>(1-2)</sup>

Nausea and vomiting which are not adequately controlled may lead to other complications, such as anorexia, hydroeletrolytic imbalance, dehydration, need for or prolonged hospitalization, quality of life impairment and negative effect on daily activities.<sup>(3)</sup> Effective treatment reduces morbidity and the risk of complications, and also prevents premature termination of chemotherapy.<sup>(4)</sup>

All chemotherapy drugs have emetogenic potential of different intensities. However, such emetogenic risk does not include nausea. The potential presented by the most commonly used drugs in breast cancer treatment protocols can be classified as: high, with a risk of vomiting of 90% (cyclophosphamide dosage over 1500mg/m² and cisplatine); moderate, with a 30% to 90% risk (cyclophosphamide dosage under 1500mg/m², epirubicin and doxorubicin); low, with a 1% to 30% risk (5-fluorouracil, paclitaxel, docetaxel, methotrexate, doxorubicin lipossomal, gemcitabina and trastuzumab); and minimal, with a risk of 10% or lower (vinorelbine). Oceans the method of the second of the s

The emetogenic risk of each cytotoxic agent for inducing nausea and vomiting determines what drug or combination of antiemetic drugs must be used. However, it is more difficult to classify the emetogenic potential of combined drugs. One example is the combination of anthracyclines with cyclophosphamide, which is the basis for many breast cancer treatment protocols. Separately, both present moderate emetogenic potential; however, their joint action results in high emetogenic potential.<sup>(6-7)</sup>

Studies indicate some factors which can favor emetic events, among them female gender, age (young), weight (the higher the body mass index – BMI – the greater the risk of presenting nausea and vomiting), drug dosage, number of cycles undergone, and light alcohol consumption. We highlight the fact that young women who do not consume alcohol, even when receiving low doses of chemotherapy drugs, as well as those with a history of vomiting during pregnancy or of motion sickness, display a greater tendency for vomiting during chemotherapy. (3,6)

Chemotherapy-induced nausea and vomiting are adverse events that should be totally controlled in most cancer patients with the development of new medications. The goal must be focused more on prevention than on

treatment, so as to improve quality of life, avoid complications, and make chemotherapy treatment easier.

Despite the advances made in controlling nausea and vomiting, the treatments currently available are not effective on all patients, and available resources need to be optimized, whether pharmacological or otherwise, in order to attain better control during treatment. The introduction of more effective drugs for control of nausea and vomiting has caused positive impacts on the quality of life of many patients. In addition, clinical practice protocols such as those provided by the American Society of Clinical Oncology, which are based on systematic literature reviews, provide recommendations for managing nausea and vomiting with medication. (6)

Even with the assistance of these protocols, the health professional who has direct contact with patients during chemotherapy must assess nausea and vomiting individually. Thus, the proposed interventions are to be personalized and adapted to each patient. The nursing professional is responsible for educating patients and their caregivers about chemotherapy, including how to prevent and manage possible toxicities.<sup>(3)</sup>

What is observed in clinical practice is that this lack of specific and standardized information during chemotherapy may be associated with lack of adequate control of adverse treatment events and, consequently, with worsening of symptoms. Based on this information, we investigated whether women with breast cancer presented nausea and vomiting during their chemotherapy and how they managed these adverse events. The goals of this study were to analyze the incidence of chemotherapy-induced nausea and vomiting in women with breast cancer, and to identify the strategies used to control such nausea and vomiting.

## **METHOD**

We conducted a descriptive cross-sectional study, assessing nausea and vomiting in women with breast cancer during neoadjuvant or adjuvant chemotherapy, carried out in the Mastology Outpatient Clinic at the Hospital das Clínicas of the Ribeirão Preto Medical School, University of São Paulo (HCFMRP-USP). The Department of Gynecology and Obstetrics of HCFMRP-USP granted permission for this study, which was approved by the Ribeirão Preto-USP Nursing School Ethics Committee (Protocol n° 1319/2011).

From the estimated 100 new breast cancer cases per year treated at this clinic, we recruited women with breast cancer who were in chemotherapy during the period between April 2009 and March 2010. We used a convenience sample and included 22 women who fulfilled the following

inclusion criteria: women over 19 years old who were in their last cycle of neoadjuvant or adjuvant chemotherapy. Criteria for exclusion were: women who could not express themselves without assistance; were diagnosed with some other type of malignant tumor; had already been treated with chemotherapy for breast cancer or some other type of malignant tumor; or were pregnant or puerperal.

For data collection, we created an instrument that gathered sociodemographic data as well as information about the chemotherapy treatment plan, antiemetic medication received before each chemotherapy cycle, incidence of nausea and vomiting during treatment, and information received for managing the consequences in daily activities. This information was obtained by interviewing participants and by reviewing their medical records. The data were organized in an Excel spreadsheet and analyzed using descriptive analysis of variables. The results are presented in charts displaying relative and absolute frequencies.

## RESULTS

During the six months of data collection, 22 women were included in the study. They were diagnosed with breast cancer, receiving their last cycle of chemotherapy, and between the ages of 31 and 70, with an average age of 50 years and standard deviation of 15.5 years.

Regarding sociodemographic variables: 50% of the women did not have high school diplomas; 50% did not have a partner; and 40.9% were in stage IIIB of the disease. Sixteen participants reported other comorbidities, the most common being arterial hypertension (27.3%), and the most common medication taken before cancer diagnosis was omeprazole (47.8%).

Among the subjects, 77.3% received neoadjuvant treatment and all participants received some type of intravenous antiemetic medication before each cycle of chemotherapy. The most commonly used drugs were ondansetron and dexamethasone for 100% of participants, followed by ranitidine, for 81.8%.

Regarding the incidence of nausea, 77.3% reported feeling it at least once during chemotherapy. For most of the subjects, the symptom occurred after the second cycle of chemotherapy, and seven women reported that it persisted throughout the entire treatment. When questioned on how long it took for the nausea to intensify, answers ranged from 6 to 192 hours (eight days). The time needed for nausea to improve also displayed much variation, which indicates the subjectivity of and the difficulty of controlling this symptom.

Vomiting was reported by 50% of participants, four of whom had already presented the symptom during the first

**Table 1 –** Distribution of women receiving chemotherapy for breast cancer, according to age, race, marital status, level of education, stage of cancer, comorbidities and medication in use. Ribeirão Preto. SP. 2012.

Variables	N	%			
Age					
31-40	4	18.2			
41-50	9	40.9			
51-60	5	22.7			
61-70	4	18.2			
Race					
White	17	77.3			
Others	5	22.7			
Marital status					
With partner	11	50			
Without partner	11	50			
Level of education					
Did not complete elementary School	11	50			
Completed elementary school	1	4.5			
Did not complete high school	4	18.2			
Completed high school	3	13.6			
Higher education diploma	3	13.6			
Stage of cancer					
IIIB	9	40.9			
IIA	8	36.4			
Other	5	22.7			
Comorbidities					
Hypertension	6	27.3			
Dyslipidemia	4	18.2			
Other	6	27.3			
None	9	40.9			
Medication used before cancer diagnosis*					
Omeprazole	11	47.8			
Antihypertensives	10	43.5			
Other	7	30.4			

Source: Proiect database.

cycle. Regarding the time elapsed before vomiting intensified, answers ranged from 24 to 120 hours (five days). This symptom improved any time between 2 and 360 hours (15 days).

Regarding symptom management, 53% of the women who presented nausea and 27.3% of those who reported

<sup>\*</sup>Participant could report more than one medication.

**Table 2 –** Distribution of women receiving chemotherapy for breast cancer, according to chemotherapy category, protocol chemotherapy drugs and intravenous antiemetic medication. Ribeirão Preto. SP. 2012.

Variables	N	%
Chemotherapy category		
Neoadjuvant	17	77.3
Adjuvant	5	22.7
Chemotherapy Protocol		
Neoadjuvant		
EC-T	7	31.8
EC-TH	7	31.8
FEC	3	13.6
Adjuvant		
EC-T	2	9.1
FEC	3	13.63
Intravenous antiemetic medication*		
Ondansetron	22	100
Dexamethasone	22	100
Ranitidine	18	81.8
Omeprazole	2	9.1
Palonosetron	9	40.9
Bromopride	1	4.5

Source: Project database

vomiting used only drug remedies. We highlight that 94.4% of women who presented nausea and 77.7% of those who presented vomiting reported having been given an orientation about taking a prescribed medicine (Table 3).

The women also reported changes in their daily lives related to the incidence of nausea and vomiting, such as not being able to carry out their usual activities and not participating in social activities due to their symptoms (Table 3).

In addition to these changes, 27.2% and 13.6%, respectively, reported loss of appetite due to nausea and vomiting; and 63.6% and 31.8%, respectively, reported other changes in eating habits due to these symptoms, such as not eating raw foods and avoiding fried foods, sweets and red meat, because they caused aversion.

Four participants reported not having received orientation regarding chemotherapy before it was initiated and 81.8% reported having received such information. However, we highlight the fact that, although the orientation given by professionals centered on drug management, when

questioned about which drugs they had taken at home in order to manage nausea and vomiting, 27.3% of participants could not provide an answer.

All of the interviewees reported having experienced other adverse effects besides nausea and vomiting. The most commonly cited were skin rashes (41%), mucositis (41%), dry mouth (31.8%), fatigue (31.8%) and alopecia (22.7%). Together with the participants, we identified which adverse effects they considered to be most stressful. Nausea was considered the most stressful for 22.7%, followed by alopecia for 18.2%, diarrhea for 18.2%, changes in taste for 18.2% and vomiting for 13.63%.

### DISCUSSION

The results of this study indicate that the women took antiemetic drugs recommended by international protocols, such as 5-hydroxytryptamine-3 antagonists (ondansetron, palonosetron), which are considered the gold standard for acute nausea and vomiting after chemotherapy. However, the general management of these events is still a problem for women with breast cancer.<sup>(9)</sup>

When antiemetic drugs are used appropriately, episodes of nausea and vomiting can be reduced considerably. In the present study, all participants received intravenous antiemetics. However, we determined that throughout the entire chemotherapy treatment, 77.3% of the women presented nausea and 50% presented vomiting, regardless of what chemotherapy protocol was used.

The data suggest that despite the use of antiemetics, there is a gap in the health team's individual evaluation of the women's symptoms and their evolution. In this sense, we observed that the drugs prescribed were all the same, with their dosage adjusted to the patient's condition and to the dosage of the chemotherapy, regardless of the symptoms presented and their frequency and intensity. Information needs to be continually circulating, in that the nursing team that cares for patients throughout each cycle of chemotherapy should collect information on the symptoms presented. They should also reinforce orientation, including the necessary precautions for avoiding additional health complications,<sup>(11)</sup> and appropriately managing those that have already occurred.

In an observational study of 143 women with breast cancer, 70% of patients presented delayed nausea, similar to this study. This type of nausea is difficult to control, regardless of which antiemetics are available and taken by patients. We emphasize the importance of using antiemetics appropriately for reducing the incidence of severe chemotherapy-induced nausea and vomiting.<sup>(12)</sup>

<sup>\*</sup>Participant may have received more than one medication per cycle.

**Table 3 –** Distribution of women receiving chemotherapy for breast cancer according to use of oral antiemetic, symptom incidence, symptom management, orientations received and types of orientation. Ribeirão Preto, SP, 2012.

Variable	Na	Nausea		Vomiting	
	N	%	N	%	
Incidence of symptom					
Yes	17	77.3	11	50	
No	5	22.7	11	50	
Therapy used					
Drug	9	53	3	27.3	
Non-drug	7*	41.1	7**	63.6	
Persistent symptoms	-	-	1	9.1	
Management orientation					
Yes	18	82	18	82	
No	4	18	4	18	
Type of orientation					
Take prescribed medication	17	94.4	14	77.7	
Change eating habits***	1	5.6	1	5.6	
Does not remember	-	-	1	5.6	
Go to a health care unit	-	-	2	11.1	
Changes in daily activities					
Interferes with daily activities					
Yes	8	36.3	4	18.2	
No	14	63.6	18	81.8	
Interferes with social activities					
Yes	7	31.8	4	18.2	
No	17	77.2	18	81.8	

Source: Project database.

We also highlight the lack of knowledge displayed by participants regarding what antiemetic medication they take at home. Lack of knowledge of patients and caretakers can lead to other unpleasant effects and interfere with the safety and guaranteed effectiveness of medications, due to their improper use.<sup>(13)</sup>

Although most participants (82%) reported having received orientation about chemotherapy and its adverse effects, we observed that only drug remedies were indicated to manage nausea and vomiting. We also found a gap in their knowledge about antiemetic medication, which may be related to the quality of information and/ or how the professional transmits it, as well as the par-

ticipant's level of education. It is agreed that information on medication must touch on its purpose, characteristics, actions and reactions, in order to improve the quality of the patient's treatment.<sup>(11)</sup>

Health professionals must be vigilant in order to evaluate and offer support to patients who present nausea and vomiting. A qualitative study which investigated the experiences of European and American patients with nausea observed that participants received little orientation from health professionals, and what they did receive was centered on drug management. The authors concluded that health professionals must educate patients about all available management strategies for nausea-related symptoms.<sup>(14)</sup>

<sup>\*</sup>Ingesting liquids, such as juice and water

<sup>\*\*</sup> Four reported that they did nothing and three ingested liquids such as juice and tea.

<sup>\*\*\*</sup> Eating every three hours for nausea and ingesting light foods for vomiting.

It is essential that nurses monitor the severity of adverse events individually and adapt antiemetic medication accordingly to minimize such events, always based on protocols of good clinical practice. The use of valid and standardized instruments such as procedures which systematize the evaluation of nausea and vomiting also helps standardize records and management of these adverse events.<sup>(15)</sup>

Dietary measures must be combined with pharmacological management of nausea and vomiting, adjusted to each patient's needs, respecting their preferences and eating habits.<sup>(16)</sup> Simple measures that can favor the management of these symptoms include spreading out meals over the day, avoiding fatty and highly seasoned foods, not lying down after meals, giving preference to cold or room temperature food, and avoiding liquids during meals (although a daily water intake of 8 to 12 cups is recommended).<sup>(16-17)</sup>

Non-pharmacological measures are also available, such as the use of phytotherapeutics, especially ginger, whose effectiveness for controlling nausea and vomiting has been demonstrated in various situations. Acupuncture, acupressure, hypnosis, relaxation, aromatherapy and yoga have also been used, and clinical studies have presented significant results regarding their use. (18) However, these procedures require specific training, as well as a suitable place for their implementation, which is not the reality of many Brazilian services that treat patients through the Unified Health System.

**Table 4** – Distribution of women receiving chemotherapy for breast cancer according to their knowledge of oral antiemetics and other medications being taken. Ribeirão Preto, 2012.

Variable	N	%
Patient's knowledge of medication		
Was able to answer	13	59.1
Was not able to answer	6	27.3
Did not take any	3	13.6
Medications *		
Ondansetron	8	
Metoclopramide	6	
Bromopride	6	
Omeprazole	4	
Dimenhydrinate	1	
Ranitidine	1	

Source: Project database.

Notwithstanding the availability of these measures in the system, or whether patients seek them spontaneously, or their combination with pharmacological measures, we reinforce the importance of educating and orienting patients and caretakers so they can successfully manage nausea and vomiting, regardless of what measure is chosen.

Protocols containing systematized orientations regarding drug management and other measures, as well as professional training, are clearly necessary. Management protocols are a set of recommendations developed systematically and based on current scientific knowledge, which help manage a specific health problem and orient the workflow, conduct and clinical procedures of health care professionals. We emphasize that the use of protocols is not without limitations, for the actions described may be restricted to preestablished procedures and may not meet the clinical demands of several different situations.<sup>(19)</sup>

In a study which assessed the challenges and application of international protocols for controlling nausea and vomiting in several European countries, from the viewpoint of nurses who work in oncology units and centers, the author states that nurses must be encouraged to work collaboratively with their peers to develop local protocols for managing these adverse events. Such protocols, different from those developed by doctors and pharmacists, must approach the patient holistically, managing nausea and vomiting with pharmacological, non-pharmacological and, above all, educational measures.<sup>(18)</sup>

When developing protocols, we must consider the perspective of patients undergoing outpatient chemotherapy in terms of their quality of life. Based on this perspective, it is possible to develop guidelines for nursing care to adequately control and manage the adverse events of chemotherapy.<sup>(20)</sup>

# CONCLUSIONS

Although 82% of participants reported having received orientation regarding management of nausea and vomiting, the information they received was limited to the use of medication and was not effective. This shows the need for continuing professional education based on good clinical practices, and for elaborating and effectively implementing protocols to standardize orientations about nursing care for women with breast cancer, aimed at evaluating and managing adverse events.

We also observed a lack of assessment and follow-up of the participants regarding adequate management of nausea and vomiting via prescribed medication and the orientation received. These data confirm the need for further

<sup>\*</sup>Participant may have received more than one medication per cycle.

studies that will accompany these women, cycle by cycle, to evaluate the incidence of gastrointestinal toxicities.

The major limitation of these studies is the small number of participants, a fact which did not allow for an association test among variables. In spite of this limitation, the results suggest that nurses who work with oncology patients must use educational methods to transmit information on treatment, including the management of any adverse events, thus favoring proper self-care, reduction of anxiety, and improvement in quality of life.

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