



## NURSE-LED TELEPHONE OF NAUSEA AND VOMITING IN CANCER PATIENTS UNDERGOING ANTINEOPLASTIC CHEMOTHERAPY WITH CISPLATIN

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### ABSTRACT

Cisplatin is an antineoplastic used in treatment of some types of cancer. However, approximately 70 to 80% of patients undergoing this treatment are at risk of nausea and vomiting. Objective: Monitoring the occurrence of nausea and vomiting in cancer patients submitted to antineoplastic chemotherapy with cisplatin from the first treatment session. Methods: It is a quantitative, prospective and cross-sectional study carried out in a university hospital, with telephone follow-up with 50 patients who underwent chemotherapy with cisplatin from the first day of the cycle with cisplatin up to 72 hours after starting treatment. Results: The onset of symptoms was more frequent in the first 24 hours (64%) and 60% of the patients reported that they were unable to perform usual activities. Conclusion: The monitoring performed by the nurses through the telephone showed the importance and the need to accompany the patients in treatment with antineoplastic of high emetogenicity as it can provide support against the symptoms of nausea and vomiting to prevent related diseases.

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### INTRODUCTION

Cisplatin is an alkylating type chemotherapeutic agent capable of forming adducts by binding to the N7 reactive site on DNA purine residues. Such changes in DNA conformation result in replication stopping and apoptosis. Evidence has shown that one of the causes of cisplatin hypersensitivity is associated with a defect in the repair system of these adducts in non-malignant cells (Dasari and Tchounwou, 2014). This chemotherapy causes damage to the epithelial cells lining the lumen of the (gastrointestinal tract) GIT, with the release of 5-hydroxytryptamine.

The encounter between this ligand and receptor of the vagal afferent neurons activates the chemoreceptor trigger zone and the center of vomiting (CV). CV then modulates the efferent signal for airway stimuli and GIT resulting in emesis (Singh *et al.*, 2016). The pathophysiology of chemotherapy-induced nausea and vomiting (NIV) is a complex process, being among the most common (70 to 80%) among cancer patients (AEOP, 2014), this incidence tends to increase (> 90%) with the use of cisplatin due to its high emetogenic potential. NIV are classified as acute when they occur in the first 24 hours, late after 24 and up to 120 hours and anticipate when occur before treatment administration, and its effective peak occurs between 48 and 72 hours (Underhill *et al.*, 2015). NIV are among the most distressing effects of chemotherapy, and when not

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adequately controlled, represent complications such as anorexia, electrolyte imbalance, need or prolongation of hospitalization; causing a negative impact on the patient's quality of life and may interfere with the continuity of treatment (Gozzo *et al.*, 2014). The high emetogenic potential of cisplatin requires a closer follow-up of patients, as these toxicities impact on quality of life, adherence to treatment and burden on health care (Herrsted *et al.*, 2016). Thus, interconsultation telephone monitoring, after the start of the first session of the antineoplastic treatment, allows more complete evaluation and orientation of these patients by the nurses (Underhill *et al.*, 2015). The objective of this study was to monitor the occurrence of nausea and vomiting in cancer patients submitted to anticancer chemotherapy with cisplatin and to identify the interference of this toxicity in daily life and the guidelines received for their selfcare.

## MATERIALS AND METHODS

It is a quantitative, prospective and cross-sectional study, carried out through the follow-up of patients submitted to the first session of antineoplastic chemotherapy with cisplatin. This study was performed at a High Complexity Oncology Care Unit of University Hospital João de Barros Barreto (UHBB), a university hospital in the Metropolitan Region of Belém (Brazil), approved under CAAE: 43943515.7.0000.0017 and developed according to Resolution CNS No. 466/2012.

### Sample

About 50 patients who underwent antineoplastic chemotherapy with cisplatin were followed between September / 2016 and September / 2017. The inclusion criteria were: (i) histopathologically positive for cancer, (ii) age > 18, (iii) patients who were starting treatment with cisplatin associated or not with another antineoplastic, (iv) access to telephone and normal hearing, and (vi) signing of the Informed Consent Term (ICT). The data collection took place in two phases guided by an interview script (form) created by the authors. Initially, socio-epidemiological and clinicopathological data were collected during the first nursing consultation at the institution's chemotherapy outpatient clinic. Subsequently, the data collection was done by non-face-to-face monitoring (via telephone) during the interview. The patient monitoring period occurred during the first 72 hours after Cisplatin administration. The connections were made for three consecutive days in order to collect information about the occurrence of nausea and vomiting, antiemetic medications used. On this occasion, the Common Terminology Criteria for Adverse Events (2010) scale was applied to analyze the degree of nausea and vomiting intensity. Additionally, it was investigated whether such toxicity altered daily life in a single enclosed question (included in the form), as well as the guidelines received by the institution's team about self-care during toxicity.

## RESULTS

**Analysis of the Data:** It was applied statistical, descriptive and inferential techniques (absolute and relative values of the studied variables) were applied. The non-parametric statistical test, Chi-square of Adherence was applied for expected proportions equal, established the level of significance = 0.05

(Inferential Analysis). The programs Microsoft Excel 2007 and Bioestat version 5.3, respectively, were used.

**Socio-epidemiological and Clinicopathological profile:** Were monitored 50 patients, approximately 54% (27) were female and 46% (23) were male, with a mean age of 53.1 years, 18 to 78 ( $\pm 15.7$ ). The majority had completed high school (36%) and half (50%) reported having a family income of 1 minimum wages (Table 1). Regarding the clinical-pathological data, the majority of patients analyzed 26% (13) had a diagnosis of gastric cancer, followed by 18% (9) by patients with esophageal cancer, 8% (4) head and neck cancer and 6% other types of cancer. The absence of comorbidities was reported in 84% of the cases, among the 16% are comorbidities such as: systemic arterial hypertension, osteoporosis, epilepsy.

**Table 1. Distribution of patients submitted to cisplatin antineoplastic chemotherapy, according to gender, age, schooling, income, comorbidities and histological type**

SOCIO-EPIDEMIOLOGICAL AND CLINICOPATHOLOGICAL PROFILE	Frequency	%
<b>GENDER</b>		
Male	23	46.0
Female	27	54.0
<b>AGE</b>		
18-32	5	10.0
33-47	10	20.0
48-62	22	44.0
63-78*	13	26.0
<b>EDUCATIONAL LEVEL</b>		
Unlettered	3	6.0
Elementary School	17	34.0
High School	30	60.0
<b>MONTHLY INCOME</b>		
none	4	8.0
230 dollars*	21	42.0
460 dollars	11	22.0
690 dollars	14	28.0
<b>COMORBIDITIES</b>		
Not*	42	84.0
Yes	8	16.0
Epilepsy	2	25.0
Hypertension	5	62.5
Osteoarthritis	1	12.5
<b>TOPOGRAPHY</b>		
Neo Gastric	13	26.0
Neo Esophagus	9	18.0
Neo Palate	4	8.0
Neo Lung	3	6.0
*Others	21	42.0

Source: UHJBB

Others: Malignant neoplasm: mouth (2/4%), cervix (2/4%), ovary (2/4%), testis (2/4%), bile ducts (2/4%), tongue base (2/4%), tongue (2/4%), rectum (2/4%), oral cavity (2/4%), duodenum (2/4%), breast (2/4%) and maxillary (2/4%). p-value < 0.0001 (X2 test)

Approximately 38% (19) of the patients did chemotherapy alone, 34% (17) underwent surgery, 26% (13) radiotherapy and only 2% (1) underwent concomitant radiochemotherapy (Table 2). In patients undergoing multidrug therapy, cisplatin and 5-fluorouracil 38% were associated (19), and neoadjuvant purpose was 36% (18). According to the medical prescriptions, the mean dose of Cisplatin administered to the patients studied was 236.55 mg / m<sup>2</sup> (32.7 - 407.7) (Table 2).

**Telephone monitoring of the incidence of chemo-induced nausea and vomiting:** Telephone monitoring occurred in the afternoon. We identified the isolated incidence of 80% (40) of nausea and 40% (20) presented only emesis, as well as the concomitance of both in 40% (20) of the cases.

**Table 2. Distribution of patients undergoing antineoplastic chemotherapy with cisplatin according to the classification of treatment associated with chemotherapy, antineoplastic associated with cisplatin, purpose of the chemotherapy treatment and dose of cisplatin**

	Frequency	%
<b>RELATED TREATMENT</b>		
Not	19	38.0
Yes	31	62.0
Surgery	17	54.8
Radiotherapy	13	41.9
Surgery and Radiotherapy	1	3.2
<b>CHEMOTHERAPY ANTINEOPLASTIC</b>		
Not	12	24.0
YES	38	76.0
5-fu	19	50.0
Etoposide	8	21.1
Gencitabine	6	15.8
Irinotecan	4	10.5
Docetaxel	1	2.6
<b>FINALITY</b>		
Adjuvant	15	39.5
Neoajuvant*	18	47.4
Curative	2	5.3
Palliative	15	39.5
<b>CISPLATIN DOSE</b>		
32.7 - 47.7	17	44.7
47.7-62.7	2	5.3
62.7-77.7	6	15.8
92.7-107.7	6	15.8
107.7-122.7	18	47.4
392.7-407.7	1	2.6

Source: UHJBB, p-value < 0.0001 (X2 test)

The occurrence of this toxicity showed peak in 24h (64%) after administration of cisplatin, with a subsequent decreasing tendency among patients (Table 3).

**Table 3. Distribution of patients submitted to antineoplastic chemotherapy with cisplatin, according to the classification of the occurrence of nausea and vomiting, degree of intensity, time of onset of symptoms and alteration of daily life**

Clinical manifestation	Frequency	%
<b>NAUSEA</b>		
Yes*	40	80.0
No	10	20.0
<b>VOMITING</b>		
Yes	20	40.0
No	30	60.0
<b>NAUSEA + VOMITING</b>		
Yes*	20	40.0
No	30	60.0
<b>NAUSEA DEGREE OF INTENSITY</b>		
0*	10	20.0
1	16	32.0
2	7	14.0
3	17	34.0
<b>VOMITING DEGREE OF INTENSITY</b>		
0	30	60.0
1	2	4.0
2	15	30.0
3	1	2.0
4	2	4.0
<b>TIME OF ONSET OF NAUSEA / VOMITING</b>		
0	10	20.0
24	32	64.0
48	6	12.0
72	2	4.0
<b>ONDANSETRON OR METOCLOPRAMIDE</b>		
Yes	22	44.0
No	21	42.0
No information	7	14.0
<b>ALTERATION OF DAILY LIFE</b>		
Yes	30	60.0
No	20	40.0

Source: UHJBB

The degree of intensity showed a greater severity (grade 3) in 34% (17) of the patients with nausea and for the variable vomit was identified a lower severity 60% (30) in a higher percentage for the degree (0) with vomiting. About the self-administration, 42% (21) of the cases used the antiemetic, they used ondansetron or metoclopramide prescribed by the physician and available in the Unified Health System of Brazil (Table 3). When asked about the change in daily life, about 75% (30) of the patients reported changes on the third day of the telephone follow-up. Regarding the guidelines received by the team, it was identified that the patients were advised regarding the use of the antiemetic, change of eating habits and emergencies (Table 4), but still additional clarifications needed to be passed on in telephone monitoring.

**Table 4. Distribution of patients undergoing anticancer chemotherapy with cisplatin, relating the occurrence of nausea and vomiting with another treatment associated with chemotherapy, association with another antineoplastic, and alteration of daily life**

RELATED TREATMENT	Nausea		p-value		
	Yes	%	No	%	
Yes	25	62.5	6	60.0	0.9997
No	15	37.5	4	40.0	
<b>ANTINEOPLASTIC</b>					
Yes	30	75.0	8	80.0	1.000
No	10	25.0	2	20.0	
<b>ALTERATIONS OF DAILY LIFE</b>					
Yes	30	75.0	0	0.0	-
No	10	25.0	10	100.0	

Source: UHJBB

## DISCUSSION

Among the 50 patients, there was a high prevalence of nausea. Approximately 80% of the patients presented nausea, 40%, vomiting and 40% both symptoms. The results of this study showed that women have expressed more of these symptoms (54%) than men monitored, and the most frequent age was in those over 61 (36%) (Table 1). This finding may be related to factors already well established in the literature as: sex and age. These are in agreement with the study with 827 Japanese, who verified the correlation of the manifestation of chemo-induced nausea and vomiting with the women being the most susceptible, and this can be explained by the genetic variability and the question of the female hormones that can predispose these symptoms (Yokoi *et al.*, 2018). Most of the participants had incomplete secondary education (36%) and a minimum wage (50%) (Table 1). In addition to the intrinsic factors, social determinants such as schooling and family income also contribute to the increase of these symptoms, because health is not restricted to biological factors, social factors are factors that negatively affect the health conditions of a population, since health problems tend to worsen between groups in socially unfavorable situations (Barreto, 2017). This low level of schooling may have corroborated the difficulty in assimilating the guidelines for the control of nausea and vomiting, because although oriented in the first time consultation, regarding the use of medication, food care and what to do in emergency situations was notable during the approaches by telephone the need to reinforce such guidelines, this implies in the difficulty to follow the guidelines received (Barreto, 2017). In view of this aspect, it is important for the health professional to review the way this information is transmitted and to invest in educational methods, since depending on the level of education the patient may be

compromised, causing harm to the prophylaxis of the NIVQ and compromising the quality of life self-care (Sá *et al.*, 2018). Besides the economic question that also undoubtedly implies self-care. And in a recent study that characterized the experience of nausea and vomiting after chemotherapy treatment, the financial situation was posed as a hindrance to carrying out the guidelines through the speech of a patients: "I use [an antiemetic] when I feel it is absolutely necessary, because it is so expensive that I cannot pay anyway" (Childs *et al.*, 2018). Another relevant finding was the onset of nausea and vomiting, mainly in the 24 hours (64%) after the beginning of the treatment ( $p < 0.0001$ ) (Table 3). In a study with 42 women submitted to moderately emetogenic chemotherapy, 90.5% of emesis episodes in the first 24 hours were found (Castro *et al.*, 2014). This data agrees with this study and highlights the importance of antiemetic protocols within what is recommended by international guidelines. The Multinational Association of Supportive Care in Cancer (MASCC) recommends the combination of antiemetics such as 5-HT3 antagonists (ondansetron), corticoids (dexamethasone) and Neurokinin-1 (NK1) receptor antagonist with for example olanzapine. This last one provides more effective protection for both acute and late nausea and vomiting (MASCC and ESMO, 2015).

In previous studies of this institution, it has been reported that adherence to the prescribed antiemetic treatment was achieved according to international recommendations. But, the prescription of dexamethasone in a dose lower than 20 mg and that NK1 is not part of the standard medication of the institution (Almeida *et al.*, 2015). This reality allows the review and adaptation of resources to universal recommendations. The association of cisplatin with 5Fu occurred in 38% of the patients (Table 2). All chemotherapeutic drugs have emetogenic potential, which varies in intensity. The potential of chemotherapeutics such as cisplatin is high (> 90%) and fluorouracil is considered low (10 to 30%), but the emetogenic potential depends on the prescribed combinations and this leads to potentiation of antineoplastic toxicities (Gozzo *et al.*, 2014). Regarding the degree of intensity, the most frequent for the nausea variables was grade 3, this fact may characterize a patient with limitations, difficulties in eating and daily activities, requiring hospitalization, considering the risk of real death, compromising self-care and the patient's usual life (AEOP, 2014). This change in habitual life was identified through verbal reporting in the study by about 75% of the patients (Table 4). This repercussion in daily life is referred to in the discourse of patients who experienced these symptoms after chemotherapy treatment and presents a multidimensional position: "It is like destroying the muscles. It is doing this over and over again." In addition to the psychosocial implications: "Isolation is an important thing." (Childs *et al.*, 2018).

Telephone monitoring is a way to contribute to a better management of the symptoms of NIVQ, in addition to the international protocols that are fundamental basis for the control of these symptoms, being essential in the support of the monitoring of the patient in real time to contribute in providing a better quality of life to the patient (NCCN, 2015; Underhill, 2015). The ability to capture health data reported by the patient in real time is considered the "gold standard" because it enables rapid clinical decision-making. The detection and early management of adverse effects caused by highly emetogenic chemotherapy is vital to improve patient outcomes, reduce

morbidity, and limit hospitalizations (Breen *et al.*, 2015). A study that carried out the telephone monitoring performed by the nurse on 300 patients undergoing antineoplastic treatment proved to be a viable option because it provided patient satisfaction in relation to nursing and the response to the adverse effects of chemotherapy showed a significant difference (Li *et al.*, 2014). This relationship of trust was shown to be very transparent at the time that spontaneous calls will occur to the telephone number used to monitor patients during the study and after the term. In an oncology clinic, the follow-up and telephone intervention by nurses to 30 patients during the acute and late treatment periods was performed as a viable and innovative form of intervention because it allows reporting symptoms outside a consultation avoiding the worsening of the clinical picture and hospitalizations (Underhill *et al.*, 2015). Some essential aspects for better management of NIV were raised, such as: telephone monitoring in the periods of highest risk of the patient presenting these symptoms was one of the reported methods, reaffirming the importance to professionals of the use of these instruments as an aid to the improving the quality of care (Hu *et al.*, 2016). The results suggest that nurses play a fundamental role in the care of patients submitted to antineoplastic chemotherapy and, therefore, in the prevention and management of CINV. Because telephone counseling can contribute to ratify information such as: guiding the correct use of prescribed medications, adequate food and emergency management, to minimize the incidence of toxicities such as nausea and vomiting.

## Conclusion

The results suggest that nurses play a fundamental role in the prevention and management of CINV, but we suggest that in addition to the guidelines already made in the periodic consultations one by one. The telephone monitoring was an important opportunity for nurses to visualize the need to emphasize nausea and vomiting-related guidelines as well as other symptoms. It is hoped to encourage the use of innovative practices for the follow-up of cancer patients with symptoms as expected after treatment with antineoplastic chemotherapy as nausea and vomiting. It is hoped to foster the creation of a risk tool for NIVQ to monitor and perform intervention in high-risk patients in addition to hospital institutions to provide the international guidelines for the management of nausea and vomiting in accessible formats to promote the continuing education of these professionals and of the other team members. The limitation found in this research was related to the small sample size, so it is expected to contribute to future research in studies with larger and homogeneous sample sizes to promote improved assessments of nausea and vomiting induced by antineoplastic chemotherapy.

## Future Scope

The limitations of this research were related to difficulties in management of CINV in the Unified Health System (SUS), a free health system of Brazil in under constant improvement. Firstly, by access to new antiemetics and current protocols (available only ondacetron). Secondly, by the access of some patients via telephone due to low socioeconomic level, isolated regions. On the other hand, the benefits of this research allowed us to reduce the gaps between the team of professionals and the patient, to be closer and identify the need for hospitalization early. Thus, the maximum degree of nausea

and death were reduced. This experience was so important that the telephone segment became a routine service.

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