Gastrointestinal Toxicities in Women During Breast Cancer Chemotherapy Treatment

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Toxicidades Gastrointestinais em Mulheres durante Tratamento Quimioterápico do Câncer de Mama

Toxicidades Gastrointestinales en Mujeres durante el Tratamiento de Quimioterapia del Cáncer de Mama

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ABSTRACT

Introduction: Chemotherapeutic agents for breast cancer treatment often cause systemic toxicities in patients, including gastrointestinal alterations. **Objective:** To identify gastrointestinal toxicities in women during breast cancer chemotherapy. **Method:** Descriptive-exploratory, quantitative and cross-sectional study using medical records of patients undergoing chemotherapy between February 2014 and February 2015 in an oncology service. After screening and selection, 194 patients were included. **Results:** In general, 457 gastrointestinal clinical manifestations were identified, of which 50.5% of the participants had up to two and 49.5% had between three and five. In addition, 74.2% had nausea, 43.3% abdominal pain, 40.7% diarrhea, 39.2% vomiting and 37.6% constipation. The occurrence of three to five toxicities was related to the occurrence of fatigue (p=0.002) and weight loss (p=0.003), as well as the number of chemotherapy cycles positively influenced the severity of nausea (p=0.041) and vomiting (p=0.023). The chemotherapeutic agents taken did not influence the occurrence of these toxicities. Lastly, nausea and vomiting (p<0.001), as well as abdominal pain and diarrhea (p=0.003) occurred. **Conclusion:** Clinical manifestations of gastrointestinal toxicity associated with chemotherapy were frequent in women with breast cancer. The simultaneous occurrence of these manifestations may be associated with fatigue and weight loss, as well as severity may be associated with the number of chemotherapy cycles.

Key words: Breast Neoplasms; Antineoplastic Agents; Drug-Related Side Effects and Adverse Reactions; Gastrointestinal Tract.

RESUMO

Introdução: Os agentes quimioterápicos para o tratamento do câncer de mama frequentemente provocam toxicidades sistêmicas nas pacientes, incluindo alterações gastrointestinais. **Objetivo:** Identificar toxicidades gastrointestinais em mulheres durante o tratamento quimioterápico do câncer de mama. **Método:** Estudo descritivo-exploratório, quantitativo e transversal, utilizando prontuários médicos de pacientes em quimioterapia entre fevereiro de 2014 e fevereiro de 2015 em um serviço de oncologia. Após rastreamento e seleção, foram incluídas 194 pacientes. **Resultados:** De modo geral, foram identificadas 457 manifestações clínicas gastrointestinais, das quais 50,5% das participantes apresentaram até duas e 49,5% apresentaram entre três e cinco. Além disso, 74,2% apresentaram náusea, 43,3% dor abdominal, 40,7% diarreia, 39,2% vômito e 37,6% constipação. A ocorrência de três a cinco toxicidades esteve relacionada com a ocorrência de fadiga (p=0,002) e perda de peso (p=0,003), bem como a quantidade de ciclos quimioterápicos influenciou positivamente na severidade de náusea (p=0,041) e vômito (p=0,023). Os agentes quimioterápicos experimentados não influenciaram nessas toxicidades. Por fim, houve náusea e vômito (p<0,001), bem como dor abdominal e diarreia (p=0,003). **Conclusão:** As manifestações clínicas de toxicidade gastrointestinal associadas à quimioterapia foram frequentes em mulheres com câncer de mama. A ocorrência simultânea dessas manifestações pode estar associada à fadiga e à perda de peso, bem como a gravidade pode estar associada à quantidade de ciclos quimioterápicos.

Palavras-chave: Neoplasias da Mama; Antineoplásicos; Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos; Trato Gastrointestinal.

RESUMEN

Introducción: Los agentes quimioterapéuticos para el tratamiento del cáncer de seno a menudo causan toxicidades sistémicas en pacientes, incluidos alteraciones gastrointestinales. **Objetivo:** Identificación de toxicidades gastrointestinales en mujeres durante la quimioterapia contra el cáncer de mama. **Método:** Estudio descriptivo-exploratorio, cuantitativo y transversal utilizando historias clínicas de pacientes sometidos a quimioterapia entre febrero de 2014 y febrero de 2015 en un servicio de oncología. Después del cribado y la selección, se incluyeron 194 pacientes. **Resultados:** En general, se identificaron 457 manifestaciones clínicas gastrointestinales, de las cuales el 50,5% de los participantes tenían hasta dos y el 49,5% tenían entre tres y cinco. Además, 74,2% tenía náuseas, 43,3% dolor abdominal, 40,7% diarrea, 39,2% vómitos y 37,6% estreñimiento. La aparición de tres a cinco toxicidades se relacionó con la aparición de fatiga (p=0,002) y pérdida de peso (p=0,003), así como el número de ciclos de quimioterapia influyó positivamente en la gravedad de las náuseas (p=0,041) y los vómitos (p=0,023). Los agentes quimioterapéuticos experimentados no influyeron en la aparición de estas toxicidades. Finalmente, la aparición de náuseas y vómitos (p<0,001), así como dolor abdominal y diarrea (p=0,003). **Conclusión:** Las manifestaciones clínicas de toxicidad gastrointestinal asociadas con la quimioterapia fueron frecuentes en mujeres con cáncer de mama. La aparición simultánea de estas manifestaciones puede estar asociada con fatiga y pérdida de peso, así como la gravedad puede estar asociada con el número de ciclos de quimioterapia.

Palabras clave: Neoplasias de la Mama; Antineoplásicos; Efectos Colaterales y Reacciones Adversas Relacionados con Medicamentos; Tracto Gastrointestinal.

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INTRODUCTION

Breast cancer treatment has been widely discussed in the literature. Today, several strategic therapeutics to treat neoplasms are available, including surgery, ionizing radiation and chemotherapic agents as neoadjuvant and/or adjuvant. The ideal therapy is the one with maximum therapeutic efficacy and minimal undesirable effects to ensure a good quality of life during oncologic treatment and minimizing the recurrence of the disease[1].

In that line, chemotherapy can promote significant reductions of recurrence and mortality by breast cancer after systemic administration of cytotoxic agents, especially in combined protocols[2]. Despite the benefits, nevertheless, chemotherapy-induced toxicities are yet challenging for patients and professionals. Among the various manifestations, adverse effects provoked by antineoplastic agents can affect the gastrointestinal tract and compromise cancer therapy[3].

The signs and symptoms of these toxicities are nausea, vomit, diarrhea, constipation, and abdominal distension further to weight loss and infections. It is anticipated that 40% or more of patients in standard dose chemotherapy develop and manifest some toxicity in the gastrointestinal tract, making it one of the most frequent and compromising of the quality of life[3,4].

The mechanisms through which chemotherapeutic agents damage the gastrointestinal mucosa are complex and multifactorial. Classically, the cellular turnover of enterocytes is altered, and damage begins. Additionally, the barrier function of the mucosa is affected provoking changes in the intestinal permeability[4], further to the production of oxygen reactive species and increase of the pro-inflammatory cytokines. These events can cause alterations in the intestinal microbiota, a condition strongly associated with gastrointestinal disorders[5].

Several chemotherapeutic agents have been utilized in the regular treatment of breast cancer, including doxorubicin, cyclophosphamide, 5-fluorouracil (5-FU) and taxanes (paclitaxel or docetaxel)[2,6]. Of these, protocols involving 5-FU have been associated with gastrointestinal toxicities in more than 80% of the patients, manifesting as diarrhea, mostly, although all these agents can damage the gastrointestinal tract[3,7].

Considering the context of health-related quality of life during chemotherapeutic treatment, it is known that sociodemographic factors, location and extension of the cancer and antineoplastic agents administered can directly impact this outcome, reinforcing the relevance of understanding these factors[8]. The objective of this study is to identify gastrointestinal toxicities in women during chemotherapeutic treatment of breast cancer.

METHOD

Descriptive-exploratory, cross-sectional, and quantitative study from medical charts of an oncology service. The theme was selected, based on the availability of the service in accepting the study, the flow of oncologic patients in chemotherapeutic treatment and for providing data for collection. At the start, 560 medical charts were identified for analysis.

The eligibility criteria were women older than 18 years of age diagnosed with breast cancer by cyto/histopathological exam and who underwent chemotherapeutic treatment between February 2014 and February 2015. Even the hard copy (non-electronic) medical charts that met the eligibility criteria, but were unable to be found in the files, with incomplete variables investigated or illegible were excluded.

The sociodemographic variables investigated were age, race (1. White; 2. Asian; 3. Brown or Black); marital status (1. single; 2. married; 3. consensual union; 4. widow; 5. separated; 6. divorced); spousal status (1. with spouse; 2. without spouse; education (1. illiterate; 2. elementary school complete; 3. high school complete; 4. university complete); household (1. urban; 2. rural); family income (1. less than 1 minimum wage; 2. between one and three minimum wages; 3. between four and five minimum wages; 4. between six and ten minimum wages; 5. more than ten minimum wages).

The clinical variables investigated were:cyto-histological diagnosis of breast cancer; time of diagnosis (1. less than six months; 2. between six and 12 months; 3. more than 12 months); extension of the disease (1. local tumor; 2. local spread; 3. distal spread); surgical procedures (1. biopsy; 2. partial mastectomy; 3. radical mastectomy); radiotherapy treatment (1. not performed; 2. until ten sessions; 3. between 11 and 20 sessions; 4. more than 20 sessions); antineoplastic protocols applied during the oncologic treatment (drugs and quantity of complete chemotherapy cycles).

The gastrointestinal toxicities evaluated were: nausea (absence or grade 1, 2 or 3); vomit (absence or grade 1 or 2); diarrhea (absence or grade 1 or 2); abdominal pain (absence or grade 1, 2 or 3); constipation (absence or grade 1, 2 or 3). The functional toxicities associated and evaluated were: fatigue (absence or grade 1, 2 or 3); weight gain (absence or grade 1, 2 or 3); or loss (absence or grade 1, 2 or 3). The scores attributed to each toxicity evaluated were based on the 4th. edition of the Common Terminology Criteria for Adverse Events (CTCAE)[9] published by the National Cancer Institute (NCI) in May 2009.

The professionals of the oncology service investigated registered qualitatively the occurrence of gastrointestinal

manifestations during the chemotherapy treatment of the patients' samples. Two nurses (investigators) of the oncology service collected and assigned the score of CTCAE to each event in days previously agreed with the oncology service in question according to its availability. A proprietary form developed by the investigators based on the study variables was utilized to register the information collected.

Based on the data collected of each patient, a spreadsheet of results was created and fed into a database in the platform/tool Google Sheets. The statistical procedures were conducted to investigate the relation among the variables with descriptive methods to verify the frequency and inferential approaches for comparison with the software PAST: Paleontological Statistics Software Package for Education and Data Analysis[10].

The Kolmogorov-Smirnov with the significance correction of Lilliefors (test of Lilliefors) was utilized to verify the normality of the set of data. The comparison among the mean scores was performed with the test H of Kruskal-Wallis with the Bonferroni correction. The distribution of categorical data was performed with the Pearson chi-square test or Fisher exact test (values expected lower than five in the contingency table), considering odds ratio and confidence interval (95%). Correlations among the variables were verified by the Spearman's correlation coefficient. The significant results were those where the *p* value was lower than 0.05.

The Institutional Review Board of the Nursing College of Ribeirão Preto of the "*Universidade de São Paulo*" approved the procedures, report number 531.146 (CAAE: 20834513.0.0000.5393). The dispositions of Ordinance 466/2012[11] on clinical trials with human subjects of the National Health Council were complied with, keeping the trustworthiness and confidentiality of the data collected. Because there was no direct contact with the study participants, the Informed Consent form was waived.

RESULTS

194 medical charts of patients with breast cancer were identified, matching the eligibility criteria to meet the objective (n=194). The patients were between 26 and 83 years of age, with mean of 53 years (SD: ±11.3). Most were Brown or Black (70.1%), married (46.4%), with partner (54.6%), no university education (83.5%), living in urban zone (82.5%) and family income equal or lower than three minimum wages (84.5%).

In addition, most of them were diagnosed with invasive ductal carcinoma in one of the breasts (83.5%) and presented a regional spread of the disease (75.3%). 59.3% had received the diagnosis of cancer for more than one year, 64.4% underwent radical mastectomy and 29.9% to more than 20 sessions of radiotherapy, 90.7% presented fatigue, 36.1% gained 5% or more of the initial weight and 18.6% lost 5% or more of the initial weight. Of the total number of participants, 457 gastrointestinal toxicities were identified and are described in Table 1.

Considering only women affected by the gastrointestinal toxicities investigated (n=172), the mean scores of each toxicity were compared by the test H of Kruskal-Wallis to verify whether the participants experienced any of these gastrointestinal signs or symptoms more severely than the other. Based on the Bonferroni correction, there was no difference among the samples (p=0.144), indicating that the mean scores did not differ among themselves significantly. Table 2 describes the occurrence of gastrointestinal toxicities according to the sociodemographic and clinical data collected.

Regarding the antineoplastic agents utilized by the participants, 23 (11.9%) utilized the protocol AC (doxorubicin and cyclophosphamide); 91 (46.9%), the protocol AC-T (doxorubicin and cyclophosphamide with subsequent taxane); 45 (23.2%), the protocols involving 5-FU and 35 (18%), other protocols. Table 3 describes the occurrence of gastrointestinal toxicities according to the chemotherapy protocols utilized.

The quantity of chemotherapy cycles was not significantly correlated with the number of cumulative quantity of gastrointestinal toxicities by the Spearman correlation test (p=0.07). On the other hand, it was observed significant, positive, and weak correlation between the severity of vomit (ρ of Spearman = 0.164 and p=0.023) and nausea (ρ de Spearman = 0.146 and p=0.041) with the quantity of chemotherapy cycles. In this same perspective, no significant correlations were observed for diarrhea (p=0.243), constipation (p=0.090) and abdominal pain (p=0.225).

Among the gastrointestinal toxicities there was significant, positive, and moderate correlation between vomit and nausea (ρ of Spearman = 0.486 and p<0.001) and significant, positive, and weak correlation between diarrhea and abdominal pain (ρ of Spearman = 0.213 and p=0.003). No significant correlations among the other combinations of possible gastrointestinal toxicities were encountered (p>0.05).

In addition, there was significant, positive, and moderate correlation between fatigue and nausea (ρ of Spearman = 0.416 and p<0.001), as well as significant, positive, and weak correlation between fatigue and constipation (ρ of Spearman = 0.265 and p<0.001), fatigue and abdominal pain (ρ of Spearman = 0.230 and p=0.001) and fatigue and vomit (ρ of Spearman =

Table 1. Stratified general occurrence in scores and mean score of the gastrointestinal toxicities identified

Gastrointestinal Toxicities	Absolute frequency	Relative frequency	Mean score†
0 to 2	98	50.5%	2.7±1.0††
3 to 5	96	49.5%	
Abdominal pain	84	43.3%	1.8±0.,8
Grade 1	35	18%	
Grade 2	31	16%	
Grade 3	18	9.3%	
Constipation	73	37.6%	1.6±0.6
Grade 1	36	18.6%	
Grade 2	33	17%	
Grade 3	4	2.1%	
Diarrhea	79	40.7%	1.6±0.5
Grade 1	35	18%	
Grade 2	44	22.7%	
Nausea	144	74.2%	1.6±0.5
Grade 1	67	34.5%	
Grade 2	75	38.7%	
Grade 3	2	1%	
Vomit	76	39.2%	1.6±0.5
Grade 1	27	13.9%	
Grade 2	49	25.3%	

(†) women who presented at least one gastrointestinal toxicity (n=172).
(††) mean of gastrointestinal toxicity in affected women (n=172).

Table 2. Occurrence of gastrointestinal toxicities according to sociodemographic and clinical data collected

Variables	G1 (0 to 2)		G2 (3 to 5)		Value of *p* (x^2)	Odds ratio	Confidence Interval (95%)
	n	%	n	%			
Participants	96	49.5	98	50.5			
Age					0.414	0.779	[0.427; 1.420]
≤ 49 years	67	34.5	63	32.5			
> 49 years	29	14.9	35	18			
Race					0.245	0.693	[0.373; 1.288]
Brown or Black	71	36.6	65	33.5			
White	25	12.9	33	17			
Marital status					0.465	1.234	[0.701; 2.172]
Married	42	21.6	48	24.7			
Others	54	27.8	50	25.8			
Spousal status					0.479	1.226	[0.696; 2.161]
With spouse	50	25.8	56	28.9			
Without spouse	46	23.7	42	21.6			
Education					0.746	1.133	[0.530; 2.422]
Complete University	15	7.7	17	8.8			
No University	81	41.8	81	41.8			

to be continued

Table 2. continuation

Variables	G1 (0 to 2)		G2 (3 to 5)		Value of *p* (x^2)	Odds ratio	Confidence Interval (95%)
	n	%	n	%			
Household					0.490	1.298	[0.616; 2.734]
Countryside	15	7.7	19	9.8			
Urban	81	41.8	79	40.7			
Family Income					0.887	0.944	[0.428; 2.081]
≤ 3 minimum wages	82	42.3	83	42.8			
> 3 minimum wages	14	7.2	15	7.7			
Time of diagnosis					0.978	1.008	[0.568; 1.787]
≤ 12 months	39	20.1	40	20.6			
> 12 months	57	29.4	58	29.9			
Extension of the disease					0.157	1.605	[0.830; 3.106]
Regional spread	68	35.1	78	40.2			
Other	28	14.4	20	10.3			
Surgery					0.731	0.902	[0.500; 1.625]
Radical mastectomy	63	32.5	62	32			
Other	33	17	36	18.6			
Radiotherapy					0.593	1.182	[0.638; 2.189]
≤ 20 sessions	27	13.9	31	16			
> 20 sessions	69	35.6	67	34.6			
Fatigue					0.002*†	5.864	[1.639; 20.98]
Yes	81	41.8	95	49			
No	15	7.7	3	1.5			
Weight gain (≥ 5%)					0.161	1.527	[0.842; 2.767]
Yes	29	15	39	20.1			
No	67	34.6	59	30.4			
Weight loss (≥ 5%)					0.003*	3.105	[1.404; 6.868]
Yes	10	5.2	26	13.4			
No	86	44.3	72	37.2			

Captions: G1: women who presented between zero and two gastrointestinal toxicities; G2: women who presented between three and five gastrointestinal toxicities.
(N) absolute frequency.
(%) relative frequency.
(x^2) chi-square test of Pearson.
(*) value of *p* lower than 0.05.
(†) exact test of Fisher.

0.181 and p=0.011). No correlations between fatigue and diarrhea (p>0.05) were encountered.

Likewise, there was significant, positive, and weak correlation between weight loss and vomit (ρ of Spearman = 0.150 and p=0.035), weight loss and nausea (ρ of Spearman = 0.156 e p=0.03) and weight loss and constipation (ρ of Spearman = 0.166 and p=0.018). No correlations between weight loss and diarrhea (p=0.282) and weight loss and abdominal pain (p=0.146) were observed.

Considering the 45 patients who submitted to the protocols with 5-FU, the number of chemotherapy cycles was not correlated significantly with the amount of cumulative gastrointestinal toxicities according to the Spearman correlation (p=0.135). Additionally, no significant correlations were observed among the gastrointestinal toxicities and the quantity of chemotherapy cycles (p>0.05 for all).

DISCUSSION

Diarrhea provoked by chemotherapeutic agents is typically a poorly recognized toxicity although is able to

Table 3. Occurrence of gastrointestinal toxicities according to the chemotherapy protocols tested.

Gastrointestinal toxicities	G3 (5-FU)		G4 (other)		Value of p (x2)	Odds ratio	Confidence interval (95%)
	n	%	n	%			
Participants	45	23.2	149	76.8			
0 to 2	25	12.9	73	37.6	0.440	0.768	[0.393; 1.502]
3 to 5	20	10.3	76	39.2			
Abdominal pain					0.859	0.941	[0.480; 1.842]
Present	20	10.3	64	33			
Absent	25	12.9	85	48.8			
Constipation					0.707	0.877	[0.443; 1.738]
Present	18	9.3	55	28.3			
Absent	27	13.9	94	48.5			
Diarrhea					0.815	0.922	[0.469; 1.814]
Present	19	9.8	60	31			
Absent	26	13.4	89	45.9			
Nausea					0.185	1.628	[0.787; 3.367]
Present	30	15.5	114	58.8			
Absent	15	7.7	35	18			
Vomit					0.206	1.578	[0.775; 3.210]
Present	14	7,2	62	32			
Absent	31	16	87	44.8			

Captions: 5-FU: 5-fluorouracil; G3: women who experienced protocols containing 5-fluorouracil; G4: women who did not experience protocols containing 5-fluorouracil.
(N) absolute frequency.
(%) relative frequency.
(x^2) chi-square test of Pearson.

influence the morbimortality associated with cancer. It is a disorder that depends on chemotherapeutic agents and regimens and is commonly associated with administration of 5-FU[3], affecting from 28% to 54% of the patients who receive capecitabine, pharmacologic precursor of this chemotherapeutic agent[12]. The incidence of this toxicity in this sample was 40.7%, however, the findings did not reveal this association with 5-FU when compared with other regimens (Table 3).

The occurrence of diarrhea during chemotherapy treatment whether low or severe, can lead to the reduction of 45% of the therapeutic dose of the patients and provoke delays in the therapeutic dosages in until 71% or discontinue chemotherapy in until 15%. In addition, diarrhea can be related to clinical conditions of dehydration and malnourishment, although gaps in understanding its mechanisms and management remain[13].

In a systematic review of studies involving capecitabine as phase I single agent and two-phase II studies of capecitabine combined with bevacizumab and lapatinib, respectively, a significant reduction of the gastrointestinal toxicity was noticed with modification of the treatment regimens of capecitabine from 14/7 to 7/7 and grade 4 toxicities, rare occurrences of diarrhea and grade 3 constipation were not found too. In addition, minimum rates ≤ 2 were noticed with diarrhea alone presenting more than 5% of incidence[12]. Only diarrhea grades 1 and 2 were encountered in the findings of the current study.

Studies involving patients with metastatic breast cancer concluded that the antineoplastic agent pertuzumab, a monoclonal antibody when combined with other cytotoxic drugs can be associated with the occurrence of diarrhea in patients with cancer, affecting up to 72% of them. At last, the strategies to circumvent this gastrointestinal toxicity involve dose adjustment, antidiarrhea drugs and nutritional support to prevent dehydration[14].

In addition to diarrhea, constipation can affect up to 41% of the patients in chemotherapy treatment with an incidence of 37.6% in this study sample. Risk factors described in the literature indicate that the alterations of gastrointestinal motility and advanced age may be associated with this toxicity[15]. Some specific chemotherapy agents present high rates of incidence of this side effect with thalidomide, cisplatin alkaloids and vinca as vincristine, vinblastine and vinorelbine, inducing in up to 80% to 90% of this symptom[3].

Constipation can cause physical damages and reduce the quality of life of the patients because the reduction of

the intestinal transit provokes the hardening of the feces, resulting in distention and abdominal pain, hemorrhoids, and rectal fissures. In addition, patients can evolve with severe complications associated with fecal impaction and potentially fatal bowel obstruction[3].

Drug management of constipation is feasible with emollients, lubricants, oral laxative, rectal-bulk forming and osmotic or saline stimulant[3]. However, the implementation of preemptive dietary interventions and nutritional education may result in reduction of the gastrointestinal effects in general, impacting positively the adherence to the chemotherapy treatment while diminishing the evasion due to intolerable side effects[16].

On the other hand, nausea and vomit are the leading gastrointestinal toxicities most feared by patients with cancer in chemotherapy treatment[17]. The chemotherapy agents-induced occurrence of nausea and vomit is related to the significant reduction of the quality of life during oncologic therapy[18], being the regular and predicted toxicities in until 70% to 80% of the patients not receiving antiemetic prophylaxis[19]. These two toxicities are continued troubles to many patients with cancer and frequently occur simultaneously. Without proper management, the occurrence of nausea and vomit can lead to low adherence and interruption of chemotherapy[17,19].

In this perspective, the comprehension of the physiopathological mechanisms, including the study of neurotransmitter and related receptors ensured the broadening of the understanding of chemotherapy-induced nausea and vomit and development of new antiemetic drugs. However, although antiemetic drugs and clinical trials to control these toxicities were disclosed in the literature, it is predicted that until 40% of the patients fail to achieve complete control[20,21] of nausea and vomit.

Risk factors for the development of chemotherapy-induced nausea and vomits involve young female patients with history of nausea and vomit during pregnancy, further to the emetogenic potential of the chemotherapeutic agents. On the other hand, electrolytic disorders and structural lesions of the esophagus or stomach are also related with the occurrence of these gastrointestinal toxicities[22]. In addition to these risk factors, a study with women in breast cancer treatment identified that 42% of the participants did not adhere to the antiemetic protocols, which was also influenced by the education level, alcohol use and previous experiences with chemotherapy agents[23].

Uysal et al.[24] investigated symptoms related to oncologic treatment of women with breast cancer. The authors concluded that the gastrointestinal symptoms are frequent in these patients including nausea, vomit, constipation, diarrhea, and weight loss corroborating the findings of this study. Similarly, they identified that the patients report inconsistencies of the symptoms provoked by the therapeutic modalities in the information about the oncologic treatment[24].

Considering the functional toxicities associated in the current investigation, the patients who lost weight over 5% had 3-fold more odds of manifesting gastrointestinal toxicities, in addition to a positive and weak correlation with symptoms of constipation, nausea and vomits. These data corroborate results found in a prospective study by Rocha et al.[25] that cachexia (complex and multifactorial syndrome involving significant alterations in the body composition) is a good predictor, based in Cox regression for the appearance of gastrointestinal toxicity provoked by chemotherapeutic treatment.

Regarding fatigue, it was found nearly 6-fold odds of presenting gastrointestinal toxicity than the patients who did not report fatigue, suggesting important association between this symptom and gastrointestinal toxicities. In addition, although not observed in these results, a longitudinal study encountered a moderate correlation between diarrhea and fatigue, indicating that patients who suffer of diarrhea are more propense to feel fatigue, further to associating with intensity, severity and impact in the quality of life[26].

The results found in this article are of associative nature and do not allow to establish a relation of cause and effect among the variables. The limitation is the absence of a temporal analysis of the manifestation and duration of gastrointestinal signs and symptoms and lack of training of the oncology service professionals in registering toxicities that should be reported prior to the application of these results, although this last topic is inherent to the nature of the study.

CONCLUSION

Clinical manifestations of gastrointestinal toxicities resulting in many severities associated with chemotherapy were frequent in women with breast cancer. The simultaneous occurrence of these manifestations can be associated with fatigue and weight loss and the severity, with the quantity of chemotherapeutic cycles. Sociodemographic variables did not correlate with this outcome. Prospective studies can establish a cause-and-effect relation and conduct a temporal analysis between the beginning of chemotherapy and the manifestation of gastrointestinal toxicities.

CONTRIBUTIONS

All the authors contributed to the study conception and/or design, collection, analysis and interpretation of

the data, wording, critical review and approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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