

Nutritional Status and Gastrointestinal Symptoms in Oncology Patients Receiving Chemotherapy

Estado Nutricional e Sintomas Gastrointestinais em Pacientes Oncológicos Submetidos à Quimioterapia

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Estado Nutricional e Sintomas Gastrointestinais em Pacientes Oncológicos Submetidos à Quimioterapia

Estado Nutricional y Síntomas Gastrointestinales en Pacientes con Cáncer Sometidos a Quimioterapia

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ABSTRACT

Introduction: The nutritional status of oncologic patients varies greatly throughout the disease, further to gastrointestinal tract related adverse effects that are common during chemotherapy treatment. **Objective:** Evaluate the nutritional status and the presence of gastrointestinal symptoms in oncologic patients undergoing chemotherapy. **Method:** Cross-sectional study with patients in treatment in the Chemotherapy Unit of the Hospital School of Pelotas Federal University (UFPel), RS, from April to July 2019. Sociodemographic data and issues related to the disease were obtained through a questionnaire. To assess the nutritional status and gastrointestinal symptoms the Patient-Generated Subjective Global Assessment was utilized. Data analysis was performed through descriptive analysis, and the association between categorical variables was verified by Pearson's chi-square test ($p < 0.05$). **Results:** A total of one hundred one patients was evaluated, mean age of 58.6 years, with higher prevalence of females (58.4%), Caucasian (77.2%), married (53.0%), belonging to class C (50.4%). Higher prevalence of gastrointestinal tract (34.6%) and breast (27.8%) cancer was found. Most patients were classified as well-nourished (66.3%), while early satiety (56.0%), xerostomia (54.0%), loss of appetite (42.0%), and nausea (37.0%) issues. No statistical association was encountered between nutritional status and any of the gastrointestinal symptoms. **Conclusion:** The nutritional status of most patients was classified as well nourished, but attention is needed for the occurrence of gastrointestinal symptoms.

Key words: Antineoplastic Agents/adverse effects; Neoplasms; Nutrition Assessment; Nutritional Status; Drug-Related Side Effects and Adverse Reactions.

RESUMO

Introdução: O estado nutricional do paciente oncológico apresenta grande variação ao longo da doença, além de efeitos adversos relacionados ao trato gastrointestinal serem comuns durante o tratamento quimioterápico. **Objetivo:** Avaliar o estado nutricional e a presença de sintomas gastrointestinais em pacientes oncológicos submetidos à quimioterapia. **Método:** Estudo transversal com pacientes em tratamento no setor de Quimioterapia do Hospital Escola da Universidade Federal de Pelotas (UFPel), RS, no período de abril a julho de 2019. Dados sociodemográficos e questões relacionadas à doença foram obtidos por meio de um questionário. Para avaliação do estado nutricional e dos sintomas gastrointestinais, utilizou-se a avaliação subjetiva global produzida pelo paciente. A análise dos dados foi realizada por meio de análise descritiva, e a associação entre variáveis categóricas, verificada pelo teste qui-quadrado de Pearson ($p < 0,05$). **Resultados:** Foram avaliados 101 pacientes, com média de idade de 58,6 anos e maior prevalência de indivíduos do sexo feminino (58,4%), de cor branca (77,2%), casados (53,0%), pertencentes à classe C (50,4%). Encontrou-se maior prevalência dos cânceres do trato gastrointestinal (34,6%) e mama (27,8%). A maioria dos pacientes foi classificada como bem nutrido (66,3%), enquanto saciedade precoce (56,0%), xerostomia (54,0%), inapetência (42,0%) e náusea (37,0%) foram os sintomas mais citados. Não foi encontrada associação estatística entre o estado nutricional e qualquer um dos sintomas gastrointestinais. **Conclusão:** O estado nutricional da maioria dos pacientes foi classificado como bem nutrido, mas necessitando de atenção para a ocorrência dos sintomas gastrointestinais. **Palavras-chave:** Antineoplásicos/efeitos adversos; Neoplasias; Avaliação Nutricional; Estado Nutricional; Efeitos Colaterais e Reações Adversas Relacionados a Medicamentos.

RESUMEN

Introducción: El estado nutricional del paciente oncológico presenta variaciones durante la enfermedad, además de los efectos adversos relacionados con el tracto gastrointestinal comunes durante la quimioterapia. **Objetivo:** Evaluar el estado nutricional y la presencia de síntomas gastrointestinales en pacientes con cáncer sometidos a quimioterapia. **Método:** Estudio transversal con pacientes tratados en el sector de quimioterapia del Hospital Escuela de la Universidad Federal de Pelotas (UFPel), RS, de abril a julio de 2019. Se obtuvieron datos sociodemográficos y relacionados con la enfermedad a través de un cuestionario. Para evaluar el estado nutricional y los síntomas gastrointestinales se utilizó la Evaluación Subjetiva Global Producida por el Paciente. Las análisis de los datos se realizó mediante análisis descriptiva, y la asociación entre variables categóricas se verificó mediante la prueba de chi-cuadrado de Pearson ($p < 0,05$). **Resultados:** Se evaluaron 101 pacientes, con edad media de 58,6 años, mayor prevalencia de mujeres (58,4%), blancos (77,2%), casados (53,0%), pertenecientes a la clase C (50,4%). Se encontró una mayor prevalencia de cánceres del tracto gastrointestinal (34,6%) y de mama (27,8%). La mayoría de los pacientes se clasificó como bien nutrido (66,3%), mientras que saciedad temprana (56,0%), boca seca (54,0%), falta de apetito (42,0%) y náuseas (37,0%) fueron los síntomas más frecuentemente. No se encontró asociación estadística entre el estado nutricional y los síntomas gastrointestinales. **Conclusión:** El estado nutricional de la mayoría de los pacientes se clasificó como bien nutrido, pero necesita la atención a presencia de síntomas gastrointestinales.

Palabras clave: Antineoplásicos/efectos adversos; Neoplasias; Evaluación Nutricional; Estado Nutricional; Efectos Colaterales y Reacciones Adversas Relacionados con Medicamentos.

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INTRODUCTION

Cancer is a large group of diseases whose characteristic is the abnormal growth of cells unable to develop their organic functions and invade organs and tissues reaching other parts of the body¹. In Brazil, cancer is the third cause of death, exceeded by circulatory diseases and external factors only. Types of more prevalence among Brazilian males are currently prostate cancer and respiratory system and breast, colon and rectum and cervical cancer in women. The higher prevalence for both genders in the country is non-melanoma cancer².

The nutritional status of the oncologic patient deserves special attention since it varies largely in the course of the treatment and of the disease. Malnutrition occurs in most patients with cancer, it is the biggest cause of morbimortality among these individuals³. Overall, tumors that cause nutritional deficit are found in the gastrointestinal tract (pancreas, esophagus and stomach), head and neck and lung mostly⁴.

On the other hand, treatment can induce weight gain since neoplastics, mainly when associated to glucocorticoids can generate hydric retention and increase of body fat⁵, as in the case of breast cancer. In addition, the dose of the medication is based in the body surface and weight and tends to be overestimated for not considering individual aspects which can lead the patient with low weight, obese and/or older to present toxicities⁶. Currently it is known the association between some types of cancer and obesity and more odds of disease relapse^{7,8}.

For a proper nutritional evaluation of the oncologic patient, it is indicated the utilization of the Patient-Generated Subject Global Assessment (PG-SGA) which ensures more sensitiveness to detect malnutrition, further to identifying the presence or not of gastrointestinal alterations impacting the nutritional status of the patients, indicating the necessity of early nutritional interventions^{5,9}.

Today, one of the most utilized antineoplastic treatment is chemotherapy which is the administration of oral or intravenous medications in order to kill malignant cells. The antineoplastics, however, are unable to differentiate normal from neoplastic tissue, can cause adverse events in different tissues, mainly those with cells of rapid proliferation^{10,11}. For having cells with intense proliferative capacity, gastrointestinal tract ends up by suffering with the unspecific toxicity of antineoplastics. Among the most frequent adverse effects of the gastrointestinal tract are vomits, nausea, oral mucositis, diarrhea, ill absorption of nutrients, intestinal constipation, food aversion and xerostomia^{5,6,12}.

As explained formerly, the nutritional condition of the oncologic patient in chemotherapy treatment can

suffer great changes, being influenced by the toxic effects directly in the gastrointestinal tract and impacting in its prognosis. The present study had the objective of evaluating the nutritional status and the presence of gastrointestinal symptoms in oncologic patients submitted to chemotherapy.

METHOD

Observational, cross-sectional study with patients in treatment at the Chemotherapy sector of School Hospital of the Federal University of Pelotas (UFPeL), RS, from April to June 2019. The Institutional Review Board of the Medical College of UFPeL approved this article which is part of a greater project titled "Food habits and quality of life of patients in chemotherapy", number 2.927.703. A student of the UFPeL Nutrition Course previously trained collected the data to avoid biases.

The sample consisted of women and men older than 18 years from the second cycle of chemotherapy who accepted to join the study by signing the Informed Consent Form (ICF) during the application of the chemotherapies. Pregnant women and patients unable to respond to the questionnaire were excluded.

The authors elaborated a questionnaire to collect the data and based in this tool, sociodemographic information of interest for the study were extracted (gender, age, skin color, marital status, occupation) and the social class as defined according to the "Associação Brasileira de Empresas de Pesquisa"¹³. In relation to the health condition, the information about the location of the primary tumor, presence or not of metastasis and chemotherapies in use (later categorized according to the class) were extracted from the charts; the patient itself reported other chronic diseases.

The Portuguese version of PG-SGA validated by Gonzalez et al.⁹ was used to evaluate the nutritional status of the subjects. It is a specific tool to determine the nutritional status of patients with cancer (regardless of the type of treatment), it is a method combining factors as changes of food intake, of weight, gastrointestinal symptoms, physical and functional alterations of the patient. The present study considered three categories of the nutritional status: A = well-nourished; B = moderately mal-nourished or suspected of malnutrition; and C = severely mal-nourished. PG-SGA also provides a total score that can be used to define specific nutritional interventions: scores from 0 to 1 indicate there is necessity of nutritional intervention at the moment; 2 to 3, a health professional must educate the patient and its parents with pharmacological intervention according to symptoms and lab tests, if appropriate; 4 to 8, indicate that the nutritionist and other professionals must

intervene; and scores above 9, that there is critical need to improve the management of symptoms and/or options of nutritional intervention⁹.

PG-SGA still contains a specific table about food intake related symptoms where the patient must indicate which appeared in the last two weeks; for this study, the gastrointestinal symptoms were considered: nausea, vomit, diarrhea, constipation, oral mucositis, xerostomia, inappetence and early satiety.

Data were entered in Microsoft Excel and the principal investigator further revised them. The association between the nutritional status (categorical evaluation) and gastrointestinal symptoms was checked according to the chi-square test of Pearson with $p < 0.05$ in the statistical software Statistical Package for the Social Sciences (SPSS) version 25.0.

RESULTS

116 subjects were invited to join the study, 15 of which refused or were unable to respond, totaling 101 patients. The mean age of the sample investigated was 58.6 ± 12.2 years and more prevalence of females, Caucasian, married of class C and retired as Table 1 portrays.

Regarding data about the disease (Table 2), there was more prevalence of primary cancers located in the gastrointestinal tract, breast and lung and in approximately one third of the patients, there was diagnosis of metastasis. Many of the patients stated they did not have other chronic diseases, but for those who did, hypertension and diabetes were reported at the most. The chemotherapies most utilized were alkylating agents followed by protocols containing two or more classes of chemotherapies.

Table 3 shows the data of nutritional status and gastrointestinal symptoms. Considering the PG-SGA nutritional status, most of the patients in chemotherapy was classified as well-nourished. When PG-SGA score was evaluated, the mean score was 13 points (standard deviation of 7.33) indicating the necessity of conduct to improve the symptoms and/or nutritional intervention. The most prevalent gastrointestinal symptoms were early satiety, xerostomia, inappetence and nausea.

No association between nutritional status (global evaluation) and any of the gastrointestinal symptoms ($p < 0.05$) was found. Likewise, no association between chemotherapies utilized and the patients' nutritional status was encountered, both for global classification of the nutritional status ($p = 0.528$) and PG-SGA ($p = 0.823$).

DISCUSSION

It was found higher proportion of female patients, married and classified as belonging to class C in the

Table 1. Sociodemographic data of patients in chemotherapeutic treatment of a public hospital in Pelotas, RS, 2019. N=101

Variable	N	% or mean (SD)
Gender		
Female	59	58.4
Male	42	41.6
Age		
Age (years)*	58.6	(12.2)
Skin color		
Caucasians	78	77.2
Non-Caucasians	23	22.8
Marital status (n=100)		
Single	23	23.0
Married	53	53.0
Divorced	12	12.0
Widow/widower	12	12.0
Social Class		
Class A	4	4.0
Classes B1 and B2	24	23.8
Classes C1 and C2	51	50.4
Classes D/E	22	21.8
Occupation (n=100)		
Retired (a)	32	32.0
Housewife	12	12.0
Servant/cooker	12	12.0
Farmer/cattle raiser	7	7.0
Professor	5	5.0
Health professional	3	3.0
Other	29	29.0

Captions: SD: Standard deviation; *Minimum age: 24 years; Maximum age: 91 years.

present study. Capelari and Ceni¹⁴ found similar data in a High Complex Oncology Center in Rio Grande do Sul northwest region, where of the 100 individuals evaluated, 56.0% were women and 60.7% of the women and 79.5% of the men were married. It was expected in this study high number of medium-low class individuals because it is a chemotherapy SUS-dedicated health unit.

For this sample, there was more prevalence of gastrointestinal tract and breast cancer regarding the location of the primary tumor. Approximately seven years ago, a study conducted in the same place evaluating 83 patients concluded that gastrointestinal tract cancers were the most prevalent too¹⁵. On its turn, breast cancer is the major neoplasm affecting women nationally with high rates of mortality².

Nearly one third of the patients referred hypertension and/or diabetes as associated diseases. Santos et al.¹⁶

Table 2. Data about the disease of patients in chemotherapeutic treatment of a public hospital in Pelotas, RS, 2019. N=101

Variable	N	%
Site of the initial tumor		
Gastrointestinal Tract	35	34.6
Intestine	22	21.8
Esophagus/stomach	7	6.9
Liver/pancreas	6	5.9
Other sites		
Breast	28	27.8
Lung	10	9.9
Gynecological	10	9.9
Prostate/testicle	7	6.9
Skin	3	3.0
Head/neck	2	2.0
Other	6	5.9
Diagnosis of metastasis		
No	69	68.3
Yes	32	31.7
Associated Diseases		
Hypertension	25	24.8
Diabetes	8	7.9
Hypertension and diabetes	4	4.0
Other	4	4.0
No comorbidities	60	59.4
Chemotherapeutics in use (classes)*		
Alkilant agents	26	26.0
Vegetal derivatives	14	14.0
Biphosphonates	10	10.0
Monoclonal antibodies	6	6.0
Coordination compounds of platinum	4	4.0
Analogues of camptothecin	1	1.0
Vegetables derivatives + alkilant agents	13	13.0
Alkilant agents+antitumor antibiotic	6	6.0
Protocols with two or more classes	20	20.0

Caption: *n = 100 (loss of one response).

who evaluated 20 female patients diagnosed with breast cancer in chemotherapy treatment in a Recife hospital, PE encountered similar data. The presence of multiple comorbidities in oncologic patients often affects the decisions about cancer treatment, they are more propense to be prescribed a reduced dose, not finishing the

Table 3. Nutritional status and gastrointestinal symptoms of patients in chemotherapeutic treatment of a public hospital in Pelotas, RS, 2019. N=101

Variable	N	%
Nutritional Status (PG-SGA)		
A	67	66.3
B	23	22.8
C	11	10.9
Gastrointestinal Symptoms*		
Inappetence	42	42.0
Nausea	37	37.0
Vomit	9	9.0
Constipation	28	28.0
Diarrhea	27	27.0
Mucositis	26	26.0
Xerostomia	54	54.0
Early satiety	56	56.0

Captions: A: well nourished; B: moderately malnourished or suspicion of malnourishment; C: severely malnourished. *One loss in this response (n=100). Gastrointestinal symptoms exceed 100% because the same patient may have reported more than one symptom.

treatment after initiated, increasing the risks of mortality and adverse events¹⁷.

About therapeutic, there are different chemotherapeutic treatment protocols according to the specificity of the disease and the patient's health conditions¹¹. Nearly one quart of the participants of this study were in use of alkilants which cause modifications to the DNA chain, restricting its replication. These chemotherapeutics are quite utilized in the treatment of breast cancers, sarcomas and myelomas and present toxicity of the mucosa (including of gastrointestinal tract)¹¹.

The nutritional status of most of the patients according to PG-SGA was classified as well-nourished. This result is positive as the consequence of malnutrition is poor quality of life, decline of tolerance to the treatment and survival, more odds of infection and increase of the costs of the health system¹⁴. Nevertheless, PG-SGA presented mean score, indicating the urgent necessity of a conduct to alleviate the symptoms and/or nutritional intervention, it is worth mentioning. Even if they are actually well-nourished, the persistence of gastrointestinal symptoms is a risk factor for malnutrition and damages related to it.

Weight and body compositions changes in oncologic patients are associated to chemotherapeutic agents, hormone therapy and their duration. In women with breast cancer, the reduction of the lean mass and increase of fat mass (sarcopenic obesity) are associated with the relapse of the disease and other comorbidities⁸. Prevention of weight

gain during and after treatment have the potential of reducing the rates of mortality because weight gain activates metabolic hormones (leptin and adiponectin) whose mechanisms inhibit apoptosis and promote cellular growth, unchaining a new tumor or favoring its progression¹⁸.

Despite the advances of chemotherapy, it is still common that patients in treatment evolve in nutritional risk¹⁹. Chemotherapies act against fast proliferation of cells of the gastrointestinal epithelium mainly, making it extremely vulnerable to their toxicity that appear as symptoms. Therefore, any structural, physiologic, biochemical or pharmacological alteration in these mucosa can worsen the patient nutritional status^{12,20}. Among the gastrointestinal symptoms, those mentioned most frequently were feeling bloated (56.0%), xerostomia (54.0%), inappetence (42.0%) and nausea (37.0%). However, other studies noticed different symptoms as the most prevalent: constipation and diarrhea (58.3%)¹⁶ and nausea (47.5%)²¹. It is emphasized still that in addition to the chemotherapies-related adverse effects, nearly 35.0% of the participants of this study had gastrointestinal cancer, which contributed for the appearance of symptoms related to the digestive system.

Xerostomia, one of the symptoms the patients reported the most was also observed in a study conducted by Mercadante et al.²² with 669 patients of which 40.4% mentioned the symptom. The third symptom quoted systematically was inappetence. Galindo et al.²³ (n=128) corroborating this finding, noticed that 61.8% of the patients had appetite alterations among which, 31.3% had inappetence and 13.3%, early satiety.

No significant association between the nutritional status and gastrointestinal symptoms was found in the present study. Saragiotto²⁴, in a retrospective longitudinal study in Hospital PUC-Campinas, with a population of adults and older adults of both genders with cancer in chemotherapeutic treatment it was noticed the absence of statistically significant differences among the variables gastrointestinal symptoms and nutritional status.

Likewise, no association among the chemotherapeutic utilized and the patients' nutritional status was found, even if considered the global classification of nutritional status (p=0.528) or the PG-SGA (p=0.823). Cyclophosphamide, iphosphamide, cisplatin and carboplatin are the most common examples of alkylating agents¹¹. In a review study¹², high doses of cisplatin, cyclophosphamide, carboplatin and other agents have high emetogenic potential, may cause nausea, vomits and consequently loss of appetite, even after one day of antineoplastic treatment.

The role of nutrition in reducing morbidities and related symptoms is vital. Nutritional screening should be

initiated at the diagnosis not only to identify malnutrition but also unintentional weight gain. Early nutritional interventions have been associated with benefits to the patient as prevention of treatment delays occurring because of severe symptoms²⁵.

The small size sample is one of this article limitations when compared to other current studies with the same population. In counterpart, the methodological thoroughness stands out as each investigator has dedicated exclusively to only one stage, attempting to standardize the data collection and analysis.

CONCLUSION

The nutritional status of most of the oncologic patients in chemotherapeutic treatment in this study was classified as well-nourished but needing attention for the occurrence of gastrointestinal symptoms. Among the symptoms with more prevalence, stand out: early satiety, xerostomia, inappetence and nausea. However, no significant association between nutritional status and gastrointestinal symptoms was found.

Future studies should investigate the nutritional status, relating chemotherapeutic toxicity symptoms to variations of weight, type of treatment, disease staging and location of the tumor as weight gain and malnutrition in individuals with cancer deserve to be verified.

CONTRIBUTIONS

Larissa Casari and Anne y Castro Marques contributed for the study conception and/or design, collection, analysis and interpretation of the data, wording and critical review. Vera Lúcia Ferreira da Silva, Otávio Augusto Moura Fernandes, Laura Moreira Goularte, Deize Elizandra Vieira Fanka, Shirley Sousa de Oliveira and Karina Sanches Machado d'Almeida contributed for the study conception and/or design, collection, analysis and interpretation of the data. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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