

Revisión

Dietetic management in gastrointestinal complications from antimalignant chemotherapy

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Abstract

Antineoplastic chemotherapy (CT) represents the systemic treatment of malignant tumors. It can be used alone or combined with surgery and / or radiotherapy. The cytotoxic agents used in chemotherapy work on both cancerous cells and noncancerous cells of the body, generally resulting in high toxicity. The biological aggressiveness of chemotherapy particularly affects rapidly replicating cells, such as those of the digestive tract, resulting in adverse effects that impair food intake, leading to compromised nutritional status and which may lead to cachexia. The main toxic effects of chemotherapy in the gastrointestinal tract include nausea, vomiting —these are the most frequent— constipation, diarrhea, xerostomia, mucositis, dysphagia and anorexia. Given the high frequency of such effects, nutritional intervention should be an integral part of cancer treatment, to maintain and/or improve the patient's nutritional status and reduce or minimize the side effects caused by treatment. Accordingly, the goal of this study is to review dietetic conduct in the process of caring for patients undergoing cancer chemotherapy.

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DIETOTERAPIA EN COMPLICACIONES GASTROINTESTINALES DE QUIMIOTERÁPICOS

Resumen

La quimioterapia (QT) representa el tratamiento anti-neoplásico sistémico de los tumores malignos. Puede ser utilizada solo o combinada con la cirugía y / o radioterapia. Los agentes quimioterápicos actúan en las células cancerosas y las células normales del cuerpo, siendo por lo general muy tóxicos. La agresividad de la quimioterapia afecta especialmente rápida replicación celular en el tracto digestivo, dando lugar a efectos adversos que impiden la ingesta de alimentos, dando lugar al estado nutricional comprometido y puede conducir a la caquexia. Los principales efectos tóxicos de la quimioterapia, el tracto gastrointestinal, como náuseas, vómitos —estos son los más frecuentes— estreñimiento, diarrea, sequedad de boca, mucositis disfagia y anorexia. Dada la alta frecuencia de tales efectos, la intervención nutricional debe ser parte integral del tratamiento del cáncer, para mantener y/o mejorar el estado nutricional del paciente y reducir o minimizar los efectos secundarios del tratamiento. En efecto, la revisión de la dietética conducta en el proceso de cuidar de los pacientes en quimioterapia contra el cáncer es el objetivo de este trabajo.

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Palabras clave: *Quimioterapia. Toxicidad. Dietoterapia. Oncología.*

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Abbreviations

IC: Intestinal constipation.
 CTZ: Chemoreceptor trigger zone.
 CT: Chemotherapy.
 RT: Radiotherapy.
 INS: Intrinsic nervous system.
 GIT: Gastrointestinal tract.

Introduction

Cancer is a generic term used to define a class of illnesses characterized by the uncontrolled, abnormal development and proliferation of cells.^{1,2} These cells divide rapidly, and if not contained, lead to the formation of malignant neoplasms.¹ The therapeutic success of cancer therapy depends on the treatment mode that is best suited to the individual patient, as well as on tumor location. The most common forms of antineoplastic treatment include chemotherapy (CT), radiotherapy (RT), and surgery.^{1,3}

CT represents a symptomatic cancer treatment, encompassing a group of substances that act on various steps of cellular metabolism, interfering in the synthesis or transcription of DNA. CT can be classified according to its purpose, as:^{1,3} a) *curative*, employed with the goal of complete control of the tumor; b) *adjuvant*, used after curative surgery, with the goal of sterilizing local or circulating cells and reducing the incidence of distant metastasis; c) *neoadjuvant*, used to obtain a reduction of the tumor, later complemented by surgery and/or radiotherapy; d) *palliative*, where it has no curative intent and is used only to improve the quality of life or survival of the patient.

Specific antineoplastic substances for tumor cells have not yet been developed—in fact, CT acts wherever these cells are found—in such a way that the cytotoxic agents act on neoplastic as well as on normal cells of the organism, at times generating severe adverse reactions.^{1,3,4} Among the most commonly affected non-cancerous cells are those with high replicative capac-

ity, such as the younger and less differentiated cells of the gastrointestinal tract (GIT). This explains the frequent occurrence of adverse effects involving the GIT, including nausea, vomiting, mucositis, xerostomia, dysphagia, anorexia, constipation and diarrhea.^{5,6,7,8}

These adverse effects are proportional to quantity, and related to the quality of the substance applied, given that chemotherapy treatment can possess differing degrees of toxicity. The adverse effects can be serious or less serious, of early or late onset, acute or chronic. In general, the first consequence of CT is a reduction in food intake, leading to a compromised nutritional status and immunological profile, a clinical context which may progress to cachexia.^{5,6,9}

Based on these considerations, the goal of this article is to review the adverse effects of CT that interfere with the nutritional status of the oncologic patient, emphasizing the importance of nutritional management during treatment.

Methods

The text was based on a literature review with defined search terms. Searches were performed in LILACS, SciELO, Cochrane library, and MEDLINE, which were chosen for their relevance to the field of health science. The search terms used were:

- Search term 1 – chemotherapy + toxicity.
- Search term 2 – chemotherapy + nutrition.
- Search term 3 – chemotherapy + vomiting.
- Search term 4 – chemotherapy + constipation.
- Search term 5 – chemotherapy + diarrhea.
- Search term 6 – chemotherapy + xerostomia.
- Search term 7 – chemotherapy + mucositis.
- Search term 8 – chemotherapy + dysphagia.
- Search term 9 – chemotherapy + anorexia.

The search undertaken allowed the acquisition of 994 items—from the use of combinations of descriptors mentioned websites— distributed according to table I.

Table I

Number of publications obtained in the literature search

Search terms	Database consulted			
	LILACS*	MEDLINE*	COCHRANE	SCIELO*
Strategy 1 (chemotherapy + toxicity)	132	105	87	31
Strategy 2 (chemotherapy + nutrition)	26	20	41	2
Strategy 3 (chemotherapy + nausea + vomiting)	25	41	38	8
Strategy 4 (chemotherapy + constipation)	4	7	10	2
Strategy 5 (chemotherapy + diarrhea)	19	31	29	9
Strategy 6 (chemotherapy + xerostomia)	19	14	4	4
Strategy 7 (chemotherapy + mucositis)	52	91	40	8
Strategy 8 (chemotherapy + dysphagia)	12	41	7	7
Strategy 9 (chemotherapy + anorexia)	22	35	18	5

*We used English terms for the MEDLINE search and Portuguese, Spanish, and English terms for the LILACS and SCIELO search. According to the methodological definition for the review, the publication dates were 01/01/2001 to 09/30/2010, and only studies involving humans were selected.

Results

From reading the summaries of studies and complete texts found —when abstracts were in agreement with the theme of the review— a careful selection process was applied to those that dealt with the following subjects: (a) gastrointestinal complications related to cancer chemotherapy; (b) the impact of these complications on dietary intake and patient nutritional status; (c) recommended nutritional therapy to treat/reduce these complications. Thirty-nine papers were finally selected, including articles, theses and dissertations that met the proposed objectives. Textbooks on nutrition, oncology and pathophysiology were also included in the bibliographic survey.

Discussion

The reading of papers and textbooks selected allowed for the delimitation of the clinical aspects and therapeutic approach to the principal disorders of the GIT related to CT —nausea and vomiting, constipation, diarrhea, xerostomia, oral mucositis, dysphagia and anorexia— which are presented below.

Nausea and vomiting

Nausea and vomiting are among the adverse effects most frequently associated with CT and are those that cause the most trepidation among patients.^{10,11} When intense, they can result in complications such as loss of appetite, dehydration, electrolytic imbalance, and compromised quality-of-life. Nausea and vomiting are sources of intense anxiety and stress and contribute to up to 10% as a predisposing factor for treatment noncompliance.^{5,11}

Nausea is an unpleasant feeling, manifested in the epigastric area or throat, which causes an imminent urge to vomit. When intense, nausea can interfere with food intake and with the patient's activity level.⁷ Vomiting consists of the violent expulsion, from the nose or mouth, of the stomach contents, from the duodenum and/or proximal jejunum. Nausea and vomiting often occur together, accompanied by signs and symptoms such as tachycardia, pallor, weakness, dizziness, and sudoresis.^{1,6}

Young, female patients without a history of excessive alcohol consumption are more prone to nausea and vomiting.⁵ Emotional factors, such as anxiety and fear —and unfavorable organic conditions such as dehydration, fasting, gastrointestinal problems, and fever— may also contribute to a higher incidence of nausea and vomiting.^{1,5}

Episodes of nausea and vomiting can be classified as acute, late-onset, and anticipatory. The acute form is the most common and occurs within the first 24 hours following CT, usually between two and six hours after infusion. Late-onset nausea and vomiting begin after 24 hours of chemotherapy administration, probably due to the continuity of the metabolic effects of the sub-

Table II
Emetic antineoplastics: emetic potential and period of maximum incidence

<i>Emetic potential</i>	<i>Medication</i>	<i>Period of maximum incidence (hours)</i>
Very high (90%)	Cisplatin	1 to 6
	Dacarbazine	1 to 4
	Streptozotocin	1 to 4
High (60-90%)	Lomustine	2 to 4
	Carmustine	2 to 6
Medium (30-60%)	Doxorubicin	4 to 6
	Daunorubicin	2 to 6
	Dactinomycin	2 to 6
Moderate (10-30%)	Cytarabine	2 to 12
	Hydroxyurea	6 to 12
	Methotrexate	4 to 8
	Etoposide	4 to 6
Low (0-10%)	Fluorouracil	4 to 8
	Vincristine	4 to 8

Source: Massunaga VM, Ayoub AC, Frias MAE, Barros MA, Kobayashi RM. Efeitos Adversos da quimioterapia: complicações no sistema digestivo. In: Ayoub AC, Farias MAE, Barros MA, Kobayashi RM. Bases de Enfermagem em Quimioterapia. São Paulo:Lamar; 2002, pp. 371-384.

stances on the central nervous system and the gastrointestinal tract. Some patients present anticipatory nausea and vomiting, which present themselves prior to medication administration.^{3,11}

Nausea and vomiting are not observed among all patients receiving CT. The occurrence and severity vary in accordance with the different emetic degrees among the various antineoplastic agents (table II).^{3,5} Roughly 30% of antineoplastic substances produce significant nausea and vomiting in treated patients, with cisplatin considered the chemotherapeutic agent with the highest emetic potential.^{6,10,12,13}

The exact mechanisms by which chemotherapeutic agents induce nausea and vomiting are not entirely known. It is believed that these symptoms are controlled by two distinct areas of the brain: the vomiting center and the chemoreceptor trigger zone (CTZ).^{3,14} As such, the vomiting center has ample control, receiving stimuli from the CTZ, located at the base of the fourth ventricle. The CTZ may be activated by the chemoreceptors present in systemic and cerebrospinal fluid circulation by mediators such as serotonin and dopamine as well as by vagal visceral impulses originating in the gastrointestinal tract in response to gastric distension as well as irritant inflammatory and ischemic phenomena.^{12,14}

Treatment

Prevention and control of nausea and vomiting is fundamental in order to avoid the numerous complica-

tions brought on by these alterations, although it is acknowledged that medication is not entirely effective for all patients. Dietetic intervention associated with antiemetic therapy is extremely important in order to enhance the therapeutic effects and provides for a more effective prevention and control.⁶

The changes in eating habits that help patients in the treatment of nausea and vomiting include:^{1,5,6,15,16}

- Eating slowly, with small and frequent meals.
- Avoiding overly spicy, fatty, and sweet foods.
- Favoring cold or warm drinks and foods, since hotter foods and drinks contribute to nausea.
- Avoiding intake of liquids during meals.
- Using well-tolerated foods with neutral odors.
- Preferring dry foods such as toasts, crackers, and cereals.
- Eating before feeling hungry, since hunger can increase nausea.
- Staying away from the kitchen during food preparation.
- Eating in a pleasant, cool environment with fresh air.

It is also important to identify negative ideas about the treatment that may generate anxiety and stress.⁵

Intestinal constipation

The definitions of intestinal constipation (IC) tend to vary significantly. Based on the frequency of evacuations established in the western world, an individual is considered constipated if there are fewer than three evacuations per week.^{1,5} However, IC should not be defined without consideration of the patient's perception.

IC is an adverse effect from CT, however it should be distinguished from complications of the neoplasm itself. In fact, subocclusion and intestinal obstruction may result in constipation, especially in patients with cancer of the pelvic, gynecological (ovarian), gastric, and pancreatic regions, arising as a result of tumor growth, plexus invasion, presence of adhesions, hernias, previous radiotherapy, peritoneal carcinomatosis, and high doses of opioids.^{17,18}

In patients undergoing CT, IC occurs due to the use of substances that interfere with intestinal motility, through toxic action on the intrinsic nervous system (INS) of the digestive tract.^{6,12,18}

IC is often accompanied by anorexia, discomfort, pain, and abdominal distension and when prolonged may cause nausea, vomiting, electrolyte imbalance, and the formation of dry, hard feces which cause pain and may lead to the formation of fecaloma.¹⁸

Suzan McMillan proposes the use of a scale for the objective assessment of constipation, in which the patient circles a number which best represents their symptoms (table III). The sum of these numbers indi-

Table III
Constipation assessment scale

	Score		
Abdominal distension	0	1	2
Change in the amount of gas expelled	0	1	2
Reduced frequency of evacuations	0	1	2
Difficulty eliminating feces	0	1	2
Sensation of rectal pressure or fullness	0	1	2
Pain in rectal and/or anal region during evacuation	0	1	2
Reduced fecal caliber	0	1	2
Need to evacuate, inability to eliminate feces	0	1	2

Source: Adapted from Bonassa EMA. Toxicidade Gastrointestinal. In: Bonassa EMA, Santana TR. Enfermagem em Terapêutica Oncológica. 3 ed. São Paulo: Atheneu; 2005, pp. 101-130.

cates the severity of this side effect, which may range from zero (no constipation) to 16 (most severe constipation).⁶

An average of 41% of patients undergoing antineoplastic treatment experience IC.¹⁶ It is known that associated factors such as advanced age, decreased mobility and physical activity, dietary errors (low-fiber diets) and psychological alterations (depression, anxiety), may increase its occurrence.⁶ The antineoplastic agents of the vinca alkaloid group—such as vincristine and vinblastine—are the most likely to cause IC.^{1,18}

Treatment

The three first lines of orientation in the treatment of IC include increased physical activity, increased water intake, and increased fiber intake.¹⁹

Constipation can be controlled with a daily fiber consumption of 25 to 35 grams for individuals over 20 years of age, and 10 to 13 grams per 1,000 calories for elderly patients.^{19,20} Fiber softens the feces and facilitates elimination; it reduces intestinal transit time, protecting the colon from cytotoxic substances; it increases fecal volume and increases microbial mass.^{19,21,22} These benefits are only relevant in the presence of liquids: the fibers absorb liquids, resulting in increased fecal volume and consequent stimulus for peristalsis. In diets with low liquid intake, dried feces adhere to the mucosa and do not come loose, or if they do, only in small quantities. It is recommended to drink two to three liters of liquid per day.^{10,12,19}

Accordingly, the nutritional recommendations for IC include:^{1,5,6,14,15,16}

- Increasing liquid intake through water, teas, coconut water, and juice.
- Drinking cold liquids, since these normally stimulate the intestinal tract.
- Increasing the consumption of whole-wheat breads, cereals, flours, and grains.

- Avoiding constipating fruits such as guava, banana and cashew, prefer laxative fruits such as papaya, plum, and orange.
- Avoiding consuming dishes containing rice cream; whenever possible, adding whole-wheat cereals, oats, linseed flour, wheat bran, granola, wheat germ, and prunes to milk, shakes, yoghurts and curds.
- Eating foods containing live lactobacilli.

Ideally, dietary fiber should be consumed in the form of foods such as fruit, vegetables, whole-wheat breads and cereals, legumes, nuts, and seeds, not only because they are rich in fibers, but also because they are excellent sources of vitamins and minerals, trace elements and antioxidants. If the patient is unable to consume adequate quantities of these foods, volume-forming agents can be used to promote regular evacuation of soft feces, including: cellulose, hemicellulose derivatives, psyllium seeds, linseed seeds/flour, plantago and osmotic agents such as lactose, magnesium hydroxide, and sorbitol.^{14,19,20,22}

At the start of a high-fiber diet, unpleasant side effects such as increased flatulence, intestinal cramps or diarrhea may occur. The gradual increase in fiber ingestion may help to avoid these symptoms.¹⁹

Diarrhea

Diarrhea may be defined as an increase in evacuation frequency, or an increase in stool volume and content, different from the normal fecal elimination pattern, and may or may not be accompanied by abdominal pain or cramps.^{5,6} It usually consists of three or more soft, liquid bowel movements per day. Roughly 75% of patients undergoing antineoplastic treatment present diarrhea.¹²

The physiopathology of diarrhea arises from the action of the antineoplastic substances on the rapidly multiplying cells of the digestive tract.¹⁸ CT interferes with the cell cycle of these rapidly dividing cells, causing a sloughing of the mucosa without adequate replacement, leading to irritation, inflammation, and functional alterations.^{1,14,18} The substances most often related to the occurrence of diarrhea in patients undergoing CT include cytarabine, actinomycin D, fluorouracil, floxuridine, topotecan, oxaliplatin, and the nitrosoureas.^{1,18} The incidence of this side effect depends not only on the substance employed but also on the dose and frequency of administration.^{6,18}

CT-related diarrhea puts the patient at risk of fluid depletion and electrolyte imbalance, conditions that are potentially fatal.⁶

Treatment

The treatment of diarrhea should begin as early as possible in order to avoid complications such as dehy-

dration, weakness, electrolyte imbalance and loss of weight. Such symptoms are common due to alterations in the flow of water and electrolytes in the digestive tract, and consequently lead to complications in the digestive, absorption and secretion mechanisms. Flattening occurs in the intestinal villus, causing difficulties in various stages of the process of digestion and absorption:

- Impaired functioning of the disaccharides (lactose, saccharose and maltose) appearing on the brush border, restricting the digestion of lactose, saccharose and less frequently maltose.
- Reduced absorption of nutrients, as the microvillus present on the superficial apical of each epithelial cell of the small intestine, the purpose of which is to supply thousands of inclines and declines leading to the expansion of the absorptive surface, are flattened.

In this context, an increase in the quantity of calories, protein, minerals, vitamins, liquids and electrolytes is essential in order to counter nutrients lost as a result of reduced digestive and absorptive function.^{21,22} Modifications to the diet are necessary to relieve the patient of the symptoms and correct nutritional deficiency.⁶

The first step consists of oral fluid and electrolyte replacement. The nutritional guidelines for diarrhea control include:^{1,6,15,16,21,22}

- Eating small and frequent meals.
- Avoiding lactose-rich foods (milk and milk products), since enterocyte lactose levels are decreased and there may be intolerance.
- Increasing liquid intake to at least three liters per day, including coconut water, isotonic, meat broth, teas, strained juices, and gelatins.
- Removing from the diet any foods that irritate or stimulate peristalsis, such as whole-wheat cereals, insoluble fibers, fried, fatty, or spicy foods, fresh fruit and raw vegetables, coffee, chocolate, citrus fruits and juices (orange, tangerine, acerola, cherry, guava, cashew, pineapple, lime, kiwi, and cachaça).
- Providing sources of soluble fiber, which assist in the control of intestinal transit by providing viscosity, as well as the possibility of producing short-chain fatty acids, important to the integrity and recovery of the intestinal mucosa.
- Avoiding flatulence-inducing foods such as garlic, onions, cabbage, broccoli, Bell peppers, sweet potato, sweets in general (caramels, bonbons, chocolate, honey, sugar), cheese, beans, peas, lentils, avocado, guava, apple, grapes, melon, watermelon, jackfruit, oranges, oats, carbonated beverages, coffee, and condiments (except salt).
- Avoiding foods that are very hot or very cold.
- Substituting sucrose for maltodextrin.

It is also important to remember the importance of a balanced diet with high levels of complex carbohydrates and a reduced amount of fat, in addition to regular physical exercise.²²

Xerostomia

Xerostomia, or dry mouth, consists of the interruption or marked reduction of salivary gland secretion.²³ Under normal conditions, 0.3 to 0.5 mL of saliva is produced per minute; xerostomia occurs when salivary flow is less than 0.1 mL per minute.²⁴ Roughly 40% of patients undergoing chemotherapy experience dry mouth, usually short-lasting, with recovery within two to eight weeks after treatment conclusion.^{14,25} The manifestations include dryness of the mouth, lip fissures, as well as papillary burning and atrophy on the dorsal surface of the tongue.^{23,24,26}

Some antineoplastic substances cause xerostomia due to competition with the receptors for the neurotransmitter acetylcholine, thus inhibiting transmission of parasympathetic nerve impulses arising from the salivary nuclei. These parasympathetic nerves are responsible for the control of the salivary glands when excited by tactile or taste stimulation from the tongue and other areas of the mouth; inhibition results in decreased salivary secretions.^{24,27}

Xerostomia affects women more frequently than men, and is also more common among the elderly. Physical examination of the affected patient typically reveals a reduction in saliva production, with a thick or foamy appearance.²⁷

Clinical findings do not always correlate with the patient's symptoms. Some patients reporting dryness of the mouth may present adequate salivary flow and oral humidity, while some patients who appear to have clinically dry mouth do not present symptoms. The lack of saliva production may be confirmed by measurement of saliva production at rest and under stimulation.²⁷

The buffering effect and the role of oral hygiene generally attributed to saliva are altered by xerostomia, thus contributing to the emergence of microbial infections, rapidly progressing dental cavities and loss of taste acuity, as well as leading to an incapacity to moisten, chew, and swallow foods. All these conditions have a profound effect on food selection and consequently on systemic nutrition.²⁴

Treatment

Patients receiving substances that trigger xerostomia should increase fluid ingestion to 25-30 mL/kg/day.^{11,19} The nutritional approach to reduce and relieve xerostomia includes:^{4,5,15,16,24}

- Preferring foods that are moist, soft, with sauces, in the form of puree, broths and icecream.

- Avoiding dry, hard foods that are hard to swallow.
- Preferring cold foods, eat acidic fruit candy, pop-sicles, and chewing gum.
- Accompanying meals with liquids, preferable acidic juices, which stimulate saliva production.
- Drinking liquids through a straw, providing less contact with the mucosa.
- Squeezing lemon juice under the tongue to increase salivation.
- Avoiding smoking and alcoholic beverages.

Other strategies include: frequent cleaning of dental prostheses, avoiding oral solutions containing alcohol since these dry out the mucosa, frequent hydration of the mouth with small sips of water and maintaining the lips moisturized with glycerin or vaseline lipstick.^{14,15,24}

The use of artificial saliva may also be beneficial to hydrate the oral mucosa. There are also medications which stimulate intact salivary glands to increase saliva production.^{24,27}

Oral mucositis

Mucositis consists of an inflammatory response of the mucous membranes to antineoplastic treatment.^{1,28,29,30} It is caused by the interference of CT on the cycles of cells that have a high rate of proliferation. It is characterized by more or less diffuse lesions on the oral mucosa, typically associated with pain, dryness, burning, bleeding and infection. Physical examination reveals erythema, erosions, and ulceration.^{26,31} Clinical manifestations generally begin with complaints of sensitivity to acidic foods and intolerance to very hot or very cold foods, starting after two to 14 days of chemotherapy. Symptoms such as dysphagia and odynophagia are common, and may lead to altered food and liquid intake.^{25,28,32}

The occurrence and severity of the lesions varies with the antineoplastic agent used, administration time, and the physical condition of the patient.^{1,5} Approximately 40% of patients undergoing CT develop mucositis in varying degrees, more often in the more intense and aggressive chemotherapeutic protocols, such as in the treatment of leukemia and lymphoma, as well as in treatment regimens that employ RT and CT simultaneously.^{1,5,14,28,33} The principal antineoplastic agents associated with mucositis include: methotrexate, 5-fluorouracil, bleomycin, doxorubicin, cisplatin, vinblastine, and vincristine.^{30,34} The degree of dysfunction of the lips, tongue, oral mucosa, teeth, and saliva according to mucositis intensity can be observed in table IV.

Risk factors for the development of mucositis include: inadequate oral hygiene, nutritional status, smoking, alcohol intake, age (young patients are more at risk), and preexisting oral conditions.^{5,32}

Chemotherapeutic agents cause mucositis through direct and indirect toxic effects on the oral mucosa.^{30,33}

Table IV
Oral cavity assessment for grading the intensity of mucositis

<i>Degree of local dysfunction</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>
<i>Lips</i>	Smooth, soft, pink, supple, moist, intact	Slightly wrinkled, dry, with red areas	Wrinkled, dry, swollen, with or without blisters, inflamed at the demarcation line	Very dry, inflamed, cracked, with ulceration and/or bleeding and/or vesicles
<i>Tongue</i>	Smooth, pink, moist, without fissures or prominent papillae, intact	Prominent papillae on base, dry, pink with reddened areas, deepening of the medial groove	Swollen, prominent papillae, redness especially at the tip and papillae (pepper-like appearance), very dry, with a film on the base, cracks	Very dry, coarse and thick, fissures and films, very red and demarcated tip, lateral vesicles, deep cracks, very swollen
<i>Oral Mucosa</i>	Smooth, pink, full, moist	Pale, slightly dry with red areas or blisters	Red, dry, inflamed, swollen, ulcerations	Very red, shiny, edematous, vesicles and ulcers
<i>Teeth and dentures</i>	Bright without membranes	Slightly opaque with discrete membranes; discretely loose	Opaque, with adhered membranes, approximately 50% of tooth enamel; loose and causing areas of irritation	Very opaque, covered with membrane; inability to use due to irritation
<i>Saliva</i>	Fluid, adequate amount	Decreased quantity	Scarce saliva, dry mouth	Thick, viscous
<i>Voice and swallowing</i>	Normal tone and quality; normal without difficulty	Slight change, lower voice, discomfort	Thick, rough and dissonant; with difficulty and/or pain	Difficulty in articulating words; almost impossible

Source: Bonassa EMA. Toxicidade Gastrointestinal. In: Bonassa EMA, Santana TR. *Enfermagem em Terapêutica Oncológica*. 3 ed. São Paulo: Atheneu; 2005. p. 101-130.

The direct effect is caused by interference of CT on the cell cycle of cells that renew themselves every seven to 14 days. Antineoplastic substances cause destruction of cells that are undergoing active division by interfering in the synthesis of DNA, RNA, and proteins. Epithelial atrophy, destruction of the basal layer of the mucosa and inhibition of cellular replacement occur, causing ulceration that may progress to massive scaling, increasing the likelihood of the development of secondary infections.^{5,28,34}

The indirect toxic effect of CT is due to myelosuppression, or suppressed immune response, making the epithelium more susceptible to ulceration, infection, necrosis and bleeding.^{33,34} The intensity of oral mucositis is directly associated with a decrease in granulocytes during the Nadir period during antineoplastic treatment, which corresponds to the time elapsed between drug administration and the occurrence of the lowest hematological.^{1,5,34} Expressed in days, the Nadir period typically occurs seven to ten days following administration of the chemotherapeutic agent.

Oral mucositis can be divided in four development phases:^{5,33,34}

1. *Inflammatory/vascular phase*: cytokine release occurs, causing local tissue damage and triggering an immune response.

2. *Epithelial phase*: antineoplastic substances act directly on the epithelial cells of the oral mucosa, resulting in a reduction of cellular replacement, atrophy, and ulceration.
3. *Ulcerative/bacterial phase*: generally occurs between seven to 10 days after CT, concomitantly to neutropenia. It is characterized by tissue erosion and secondary bacterial colonization, leading to a new release of cytokines and, consequently, greater tissue damage.
4. *Healing phase*: resolution of neutropenia occurs, epithelial renovation and proliferation and the reestablishment of the local microbiota.

Treatment

The treatment goal for oral mucositis is the prevention of complications such as secondary infections and bleeding, relief of local pain and discomfort, maintenance of the integrity of the oral mucosa, and adequate caloric intake. Accordingly, the following overall guidelines apply:^{1,5,6,14}

- Perform a daily, careful evaluation of the oral cavity of patients undergoing CT, before and after administration of the chemotherapeutic medication.

Table V
Chemotherapy-related dysphagia toxicity scale, according to the Common Toxicity Criteria (CTC), 1982

Grade 0	None
Grade 1	Able to eat regular diet
Grade 2	Requires predominantly pasty, soft, or liquid diet
Grade 3	Requires enteral feeding, Intravenous hydration or hyperalimentation
Grade 4	Complete obstruction (cannot swallow saliva), ulceration with bleeding induced by non-trauma or perforation

Source: Adapted from Dias MCG. Repercussão da terapia nutricional em quimio e radioterapia. In: Waitzberg DL. *Dieta, Nutrição e Câncer*. São Paulo: Atheneu; 2004, pp. 450-460.

- Emphasize to the patient and the family the importance of maintaining good oral hygiene in the prevention of mucositis-related complications.
- Advise the patient on the most appropriate alternatives for mouthwashes, such as saline solutions of sodium chloride and alkaline solutions containing sodium bicarbonate, and also those that are contraindicated, such as commercial solutions containing alcoholic diluents.
- Advise the patient to avoid smoking.
- Promote local hydration with cacao butter or vaseline-based creams.
- Advise the doctor about any change in the evolution of the mucositis, as worsening may warrant dose reduction or suspension of the chemotherapeutic treatment.
- Relieve pain with the use of topical or systemic anesthetics, according to medical prescriptions.
- Advise the patient to avoid dental treatment during the Nadir period of the antineoplastic substances.
- Inform the patient and family of the possibility of mucositis occurrence and of the resources available to alleviate this side effect.

The nutritional guidelines include:^{1,5,6,14,15,16,22}

- Individual dietary adaptation in terms of consistency, flavor, acidity, and temperature.
- Frequent small meals, favoring foods that are rich in proteins and calories.
- Explaining to the patient that palate changes are common and may anticipate the signs and symptoms of mucositis.
- Offering foods that are pasty or semi-liquid in consistency, easy to chew and swallow, with mild flavors and served at room temperature (not overly hot or cold).
- Excluding from the diet any foods that irritate the mucosa, such as salt or seasonings, peppery spices, and acids.
- Ingesting soft foods with purees, creams, and smoothies made with milk and fruit.
- Drinking smoothies and juices through a straw since this makes swallowing easier.
- Encouraging intake of liquids (about two to three liters per day).

Dysphagia

Dysphagia is the difficulty—or even the impossibility—to swallow food normally. When there is pain associated with the process of swallowing, the term odynophagia is used.^{35,36,37,38} Some symptoms associated with dysphagia include choking or coughing after meals, a choking sensation, abnormal sensation of food lodged in the back of the throat, and gurgling voice quality.^{35,36,37,39} There is no concrete data on the prevalence of dysphagia in patients undergoing CT.

In the patient undergoing CT, dysphagia is characterized by changes in the preparatory, oral, and pharyngeal phases of swallowing. Antineoplastic agents interfere with the cell cycle of the quickly-renewed cells of the GIT, leading to symptoms such as xerostomia, mucositis, dysgeusia and stomatitis, which alter oral and pharyngeal sensitivity, resulting in less stimulation of the swallowing center, with an increase in pharyngeal transit time for food, reduced laryngeal elevation, and laryngeal penetrations or aspirations, among others.^{16,25,27,35}

Using the criteria established by the National Cancer Institute, table V presents dysphagia intensity assessments in oncologic patients undergoing antineoplastic treatment.¹⁶

Treatment

The dietary strategies to facilitate swallowing and prevent aspiration of food should include the following aspects:^{5,15,16,35,40,41}

- Adjusting food consistency by individual tolerance.
- Making frequent, small-volume meals, avoid foods in extreme temperatures.
- Excluding irritant foods; increase consumption of foods rich in proteins and calories.
- Maintaining upright posture during and within the 30 minutes after meals to reduce the risk of aspiration; avoid environmental distractions and conversations during the meal.
- Adding thickening agents to food—to avoid aspiration—such as non-fat milk powder, corn starch,

modular carbohydrate supplements, or commercial thickeners containing a modified corn starch-based thickening agent.

- Encouraging the patient to focus on their eating helps to avoid choking.

Anorexia

Anorexia is the most frequent complication associated with cancer, being present in 24% of patients at diagnosis and reaching 80% in the advanced disease stage.^{42,43,44,45} It affects roughly 66% of patients undergoing chemotherapy.^{1,5,46} It consists of a loss of appetite, early satiety, a combination of both, or a change in food.^{42,44,47,48,49} The effects of anorexia progress rapidly and are difficult to reverse, making early intervention a worthwhile strategy with regards to patient nutritional status.^{43,44,48,49,50}

Some antineoplastic medications commonly associated with anorexia are: carboplatin, cytarabine, dacarbazine, fluorouracil, hydroxyurea, methotrexate, and bleomycin sulphate.¹

The intensity of this side effect is related to several factors, such as: dose and frequency of administrations, overall status of the patient, presence of pain, psychological factors including anxiety, fear, depression, and use of other medications associated with chemotherapeutic treatment.^{1,17,51,52}

Virtually all chemotherapeutic agents are associated with anorexia. At effective therapeutic dosage levels, these drugs in general present an acute anorexic effect due to their actions in the central firing zone of the food avoidance chemoreceptor.^{34,39} However, food intake can diminish long-term due to symptoms such as nausea and vomiting, food aversions, impaired oral function (mucositis, dysphagia, and xerostomia), dysgeusia and ageusia, gastric irritation and GIT alterations (slow gastric emptying).^{5,42,44,47,52,53}

Dysgeusia is one of the symptoms most commonly related to loss of appetite, and consists of a change in varying degrees in taste sensation. It is often described by patients as an unpleasant, characteristically metallic or putrid taste that lingers in the mouth.^{54,55,56,57}

The risks arising from medication-induced loss of appetite depend on both the primary toxicity of the substance and on the secondary effects of appetite loss. These include not only weight loss, but also specific nutrient deficiencies.^{16,51}

Treatment

Some dietary strategies to reduce the discomfort associated with food intake and increase energetic nutrient consumption include:^{5,14,15,16,43,58}

- Reinforcing the first meals of the day, since anorexia is often less intense earlier in the day.

- Eating slowly, having frequent, low-volume meals, and avoiding fluid intake during meals (these measures aim to counter early satiety and gastric bloating which, when associated with loss of appetite, limit dietary intake).
- Avoiding frequent repetitions of foods.
- Avoiding excess fat, because it increases satiety and delays gastric emptying.
- Facilitating the choice of favorite foods.
- High-calorie and high-protein nutritional supplements offer complementation of great value.
- Encouraging oral hygiene before meals to improve the palate.
- Eating whenever hungry.
- Appetite stimulants should be administered according to medical criteria.

Increasing the dietary caloric and protein content is also an important strategy, utilizing the following guidelines:⁴⁷

- *Caloric increase:* fruit jams in yoghurt or milk; condensed milk or honey in fruit salad; starchy foods like potato, yam, and manioc in soups and salads; porridge made with milk and thickener.
- *Protein increase:* parmesan or other cheese in soup; powdered milk added to liquid milk; eggs added to some foods such as soups; omelets enriched with cheese or milk; beef, chicken, or fish stocks in foods like soups, rice, beans; shredded chicken, beef, or fish in salads or sandwiches, juice with milk.

Other important measures include:^{5,6,15,16,43,47}

- Meals should be eaten in a quiet place, with good chewing of the food.
- The patient should stay away from the place where the food is prepared so that the odors produced do not interfere with meals.
- Physical exercise, adapted for the tolerance of each patient, should be performed before each meal, if possible, as this may increase appetite.

Conclusion

Nutritional therapy is a fundamental part of the treatment of oncologic patients undergoing chemotherapy, as dietetic prescription, in addition to providing for the patients nutritional needs, should, above all, provide pleasure and comfort.

The nutritionist who works with patients undergoing CT should establish an individualized nutritional treatment plan and schedule the dietary therapeutic approach with periodic reviews, which may minimize symptoms, leading to a reduction of complications, duration of hospital stay, and costs. This approach,

constructed within a multidisciplinary team—and with a central premise of comprehensive care— may represent a significant improvement in patient quality of life.

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