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ORIGINAL ARTICLE

Oral mucositis evolution after nutritional intervention in cancer patients under palliative care*

Evolução da mucosite oral após intervenção nutricional em pacientes oncológicos no serviço de cuidados paliativos

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SUMMARY

BACKGROUND AND OBJECTIVES: Oral mucositis symptoms bring severe consequences to patients' quality of life and may require partial or complete interruption of cancer treatment. This study aimed at evaluating oral mucositis evolution in cancer patients under palliative care after medical and nutritional intervention and orientation, in addition to analyzing how mucositis interferes with patients' food ingestion.

METHOD: Participated in this study 23 patients under palliative care who answered questionnaires with questions regarding number of meals/day, meals consistency, drugs used, oral complaints and life habits. Patients were individually interviewed in the flrst visit and 15 days after by the physician and the nutritionist considering disease diagnosis and symptoms.

RESULTS: 65.2% of patients had mucositis grade I and 46.6% of them consumed solid food. 4.3% of patients had mucositis grade IV and all of them consumed liquid food. At return, 73.9% of patients had no mucositis and from them, 64.7% reported no restriction with regard to diet consistency. Dry mouth had the highest incidence at flrst visit (86.9%) being decreased to 34.7% at treatment completion. Candidiasis, diagnosed in 43.4% of patients was decreased to 13% after the intervention.

CONCLUSION: Oral mucositis is very common among cancer patients and the multiprofessional approach is critical for the efflcient management of patients under palliative care, respecting their autonomy and quality of life.

Keywords: Nutritional physiology, Oncology, Oral mucositis, Palliative care.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A sintomatologia da mucosite oral traz graves consequências para a qualidade de vida dos pacientes, podendo exigir interrupção parcial ou completa do tratamento antineoplásico. O objetivo deste estudo foi avaliar a evolução da mucosite oral em pacientes oncológicos atendidos pelo serviço de cuidados paliativos, após a intervenção e orientação médica e nutricional, além de analisar de que forma a mucosite interfere na ingestão alimentar dos pacientes.

MÉTODO: Foram avaliados 23 pacientes em cuidados paliativos, que responderam a questionários compostos por questões relacionadas ao número de refeições/dia, consistência das refeições, medicamentos em uso, queixas orais e hábitos de vida. As entrevistas foram realizadas no primeiro atendimento e após 15 dias. Os atendimentos foram realizados pela nutricionista e pela médica, de maneira individualizada, considerando o diagnóstico da doença e sintomas apresentados.

RESULTADOS: 65,2% dos pacientes apresentaram mucosite grau I e 46,6% destes consumiam alimentos de consistência sólida. 4,3% dos pacientes apresentaram mucosite grau IV com 100% destes deglutindo alimentos de consistência líquida. No retorno dos pacientes 73,9% não apresentaram mucosite e destes 64,7% referiram não ter restrições à consistência da dieta. Xerostomia foi que apresentou maior incidência no primeiro atendimento, 86,9% reduzindo para 34,7% no flnal do tratamento. A

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candidíase diagnosticada em 43,4% dos pacientes reduziu para 13% após a intervenção.
CONCLUSÃO: A mucosite oral é intercorrência muito comum nos pacientes em tratamento oncológico e a atuação multiproflssional é fundamental para o manuseio eflciente dos pacientes em cuidados paliativos, respeitando sua autonomia e qualidade de vida.
Descritores: Assistência paliativa, Fisiologia nutricional, Mucosite oral, Oncologia.

INTRODUCTION

Cancer is the second major cause of mortality in Brazil, being responsible for 13% of all deaths worldwide. An incidence of 518,510 new cancer cases is estimated for 2012 and from these, 90,940 will be in the Southern region[1].
Every year, medicine brings new advances with regard to cancer management, however many patients only look for medical assistance when their disease is advanced, requiring speciflc therapeutic care for these patients who can no longer be cured[2]. Patients under palliative care may have different symptoms associated to the disease or to the use of drugs and which directly interfere with food consumption, such as inappetence[2].
Oral mucositis is consequence of a local in‡ammatory process and cancer treatments, such as radiotherapy and chemotherapy for head and neck tumors, are a major cause of this disease[4]. It is also related to the most important acute side-effect of oral radiotherapy[5].
Mucositis pathophysiology is divided into 4 phases: in‡ammatory, epithelial, ulcerative and curative. In the in‡ammatory phase, the epithelial tissue releases interleukin 1 (IL-1), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-alpha) increasing local vascularization. In the epithelial phase there is decreased cells renewal due to radiotherapy and chemotherapy, which ulcerate the epithelium. The ulcerative phase itself occurs when there is colonization by micro-organisms and intensiflcation of lesions. Finally, there is the curative phase, corresponding to cell renewal followed by mucositis healing[4].
Oral mucositis symptoms bring severe consequences to patients' quality of life. Major signs and symptoms are mucosal ulceration with severe pain, difflculty to eat, difflculty to talk and to make oral hygiene, and the presence of opportunistic infections[4].
Severe oral mucositis may also require partial or total interruption of cancer treatment, such as radiotherapy, before the planned schedule is complete, increasing the risk of tumor cells proliferation and making difflcult to control the disease[6]. In patients under chemotherapy, mucositis in general appears in non-keratinized mucosa of the ventral face of the tongue, of mouth ‡oor, of soft palate and also in the cheek mucosa.
In patients under head and neck radiotherapy, in‡ammation may affect both keratinized and non-keratinized mucosa. Alcohol and tobacco, chemotherapy, fungal infections and poor oral hygiene may increase the incidence or worsen mucositis[6].
Patients with oral mucositis may have odynophagia, leading to malnutrition, dehydration, bacterial and fungal infections, mood and sleep disorders. It is believed that chamomile (*Chamomilla recutita*) has anti-in‡ammatory properties in wound healing, bacteriostatic and antiseptic activities. There are evidences that chamomile essence has strong activity against Gram-positive and Gram-negative bacteria[7].
This study aimed at evaluating the evolution of oral mucositis in cancer patients under palliative care, after medical and nutritional intervention and guidance, in addition to analyzing how the severity of mucositis interferes with patients' food ingestion.

METHOD

We have evaluated 42 patients, however 19 did not complete the study for not having clinical conditions to remain in the research.
So, the study continued with 23 patients admitted to the outpatient setting of the Palliative Care Service, Hospital Erasto Gaertner (HEG). Sample was delimited according to the demand of oral mucositis patients from August 2010 to September 2011. All patients were informed about the study methodology and objectives and only those who agreed to participate by signing the Free and Informed Consent Term were included in the study.
Inclusion criteria were: cancer patients without curative possibilities, with oral mucositis, aged 18 years or above and functional capacity equal to or higher than 40% by the Karnofsky scale. Patients not agreeing to participate in the study or not meeting remaining inclusion criteria were excluded. Karnofsky scale is a tool to evaluate patients' performance through physical ability and self-sufflciency, with scores varying from 10% to 100%.
Individuals with functional capacity equal to or below 40% by the Karnofsky scale were excluded for not having clinical conditions to follow medical and nutritional guidelines.
In the flrst visit, patients have answered a questionnaire with questions regarding the number of meals/day,

meals consistency (liquid, liquid-pasty, pasty, cooked or solid), drugs used and oral complaints such as dysgesia, dry mouth, appetite loss, anorexia and candidiasis. They were also asked whether they had already been submitted to chemotherapy and/or radiotherapy, whether they were currently smokers or drinkers. This same questionnaire has recorded patients' medical diagnosis of neoplasias.

The presence of mucositis was evaluated by inspection of the oral cavity by the physician and was classifled according to the grade of mucositis developed by the World Health Organization (WHO), which is clinically divided into 4 groups: Group 1 (G1): burning and erythema; Group 2 (G2): erythema, ulcers and patient able to swallow solid food; Group 3 (G3): ulcers, extensive erythema and patient unable to swallow solid food; and Group 4 (G4): ulcer, extensive mucositis and swallowing is impossible[9].

Visual analog scale was used to evaluate oral cavity pain, considering zero no pain, 1 to 3 mild pain, 4 to 6 moderate pain and 5 to 10 severe pain.

Patients were re-evaluated 15 days later, as during the flrst visit, again answering the questionnaire and being submitted to new oral cavity inspection.

Patients were interviewed by the same researcher in both visits, and the physician has classifled each patient by Karnofsky functional capacity scale (KPS).

All patients received dietary intervention, regardless of their grade of mucositis, contemplating the following aspects: mouthwashes with cold industrialized chamomile tea three times a day; avoid very acid, dry, hard or spicy food; restrict salt; avoid very hot food or preparations.

Medical approach was individualized considering disease diagnosis and symptoms. In the presence of candidiasis, in addition to dietary guidelines, 5 mL nystatin was prescribed, corresponding to 1000,000 UI every 6 hours for 10 days if mild or moderate infection, and 100 mg ‡uconazole/day for seven days if severe infection[10], according to the palliative care service routine.

Data were recorded in Microsoft Excel® and were analyzed by the SPSS 17.0 system, initially through descriptive statistics, frequency and percentage. Chi-square test was used to compare efflcacies between beginning and end of the study for the variables: grade of mucositis, dysgeusia, dry mouth, appetite loss, anorexia and candidiasis, with signiflcance level of 5%.

Wilcoxon's test for paired data was used to compare oral cavity pain decrease.

This study was approved by the Research Ethics Committee, Hospital Erasto Gaertner (process 2031/2011).

RESULTS

From 23 patients, 13 were males (56.5%) and 10 females (43.4%). Mean age was 61 years varying from 24 to 85 years of age.

Most frequent neoplasias were urinary tract (26%), gastrointestinal tract (21.7%), gynecological (13%) and respiratory (13%), followed by head and neck tumors (8.6%) and skin tumors (8.6%). Breast cancer corresponded to 4.3% and hematopoietic system cancer to 4.3%.

As to the number of meals, 8.6% of patients had only two meals/day in the beginning of the treatment, decreasing to 4.3% at the end of 15 days. Three meals a day were taken by 17.3% of patients both before and after the intervention. Patients reporting four meals/day corresponded to 43.4% in the flrst visit and to 34.7% in the second evaluation. At the end of the intervention there were a higher number of patients having flve meals/day, from 26% to 30.4%. There has been an increase in the number of individuals having six meals/day at the end of the intervention, from 4.3% to 13%.

During the flrst evaluation (Table 1) there has been grade I mucositis in 65.2% of patients and from them, 46.6% would eat solid food. From 17.3% with grade II mucositis, 50% had pasty food. Grade III mucositis was represented by 13% of patients, and from them 66% corresponded to patients with liquid ingestion and 33.3% with liquid-pasty ingestion. Only 4.3% of patients had grade IV mucositis and 100% of them had liquid food.

At return, after 15 days of treatment and nutritional guidance, 73.9% of patients had no oral mucositis and from them, 64.7% referred no restriction to diet consistency. Grade I mucositis was found in 13% of patients, without prevalence of any consistency. Grade II mucositis was found in 8.6% of patients and from them, 50% reported ingesting liquid food and 50% reported ingesting free consistency food. Grade III mucositis represented 4.3% of patients with 100% of them ingesting pasty food. No grade IV mucositis was detected during re-evaluation (Table 1).

From major oral complaints (Table 2), dry mouth had the highest incidence during flrst visit with 86.9%, decreasing to 34.7% at the end of the intervention ($p < 0.001$). Second major complaint was dysgeusia, with 60.8% and decreasing to 8.6% ($p < 0.01$), followed by appetite loss with 47.8% and decreasing to 13% ($p < 0.05$). Anorexia had the lowest difference between both visits (43.4% to 30.4%).

Candidiasis was diagnosed in 43.4% of patients

Table 1 – Grade of mucositis and diet consistency in flrst and second visits.

Mucositis Classifl cation	1st Visit		2nd Visit	
	% of Patients	Prevailing Diet Consistency	% of Patients	Prevailing Diet Consistency
No mucositis	Zero	-	73,9%	Solid (64,7%)
Grade I Mucositis	65,2%	Solid (46,6%)	13%	Liquid (33,3%) Pasty (33,3%) Solid (33,3%)
Grade II Mucositis	17,3%	Pasty (50%)	8,6%	Liquid (50%) Solid (50%)
Grade III Mucositis	13%	Liquid (66,6%)	4,3%	Pasty (100%)
Grade IV Mucositis	4,3%	Liquid (100%)	Zero	-

during first evaluation and after the intervention it decreased to 13%.

Oral cavity pain during flrst evaluation was classifled as absent in 21.74% of patients, mild in 52.18%, moderate in 17.39% and severe in 8.69%. No patient had pain during second evaluation ($p < 0.001$).

With regard to previous cancer treatment in a period shorter than one year, 39.1% of patients received chemotherapy and 21.7% radiotherapy, however all patients had already interrupted these treatments for more than 30 days.

During the study, systemic antibiotics were used by 4.3% of patients, steroids by 69.5%, antifungal by 26% and anti-in‡ammatory drugs by 21.7%.

In terms of life habits, no patient has reported ingesting alcoholic beverages and 30.4% were tobacco-dependent during the treatment.

Table 2 – Patients' oral complaints

Complaints	1st Visit	2nd Visit
Dry mouth	86,9%	34,7%
Disgeusia	60,8%	8,6%
Loss of appetite	47,8%	13%
Anorexia	43,4%	30,4%
Candidiasis	43,4%	13%

DISCUSSION

Palliative care services involve all types of tumors. So, results obtained with regard to types of cancer as compared to the grade of mucositis were not statistically signifl cant in our study, probably due to the small number of individuals with each type of tumor.

Leukemia and lymphoma are examples of malignant tumors causing bone marrow suppression and tend to be more frequently associated to oral complications[11].

In our study, 31.7% of patients had previous chemotherapy and 27.7% previous radiotherapy. Cancer patients very often start their treatment with the association of therapies such as surgery and/or radiotherapy and/or chemotherapy[5].

Treatment-related factors, such as type of radiation, drug used and daily doses are generally described with regard to their effects on normal tissues. Age, clinical and dental status are factors inherent to each patient and have been associated to the presence of oral mucositis[12].

Our study has observed that a few number of patients had six meals a day in the beginning of the treatment, increasing to 13% at the end of the intervention. These data are in line with the literature according to which oral mucositis affects basic human activities, such as food ingestion and communication, and may impair interpersonal and social relationships[13].

In our study, most patients who started the treatment with grade I mucositis did not need changes in diet con-

sistency. However, as from grade II, most patients have used modifled diets for better food ingestion, including cooked, pasty or liquid food.

Patients' guidance about the type of food during this rehabilitation period is critical to prevent further worsening of the in‡ammatory process. We have observed major improvement in diet consistency during both visits, associated to decreased grade of mucositis and less pain, with no pain during second evaluation, allowing patients to ingest more variety and quantity of food following an adequate diet.

Information about type of food, consistency, acid and spicy food restriction is necessary to improve symptoms. These guidelines depend on the severity of the lesions and it is essential that the diet-therapeutic approach respects individual wills[3].

During the second visit, there has been increased number of patients ingesting food without consistency restrictions. In addition, there was no mucositis in 73% of patients, thus assuring better quality of life.

From patients' complaints, dry mouth was prevalent in 86.9% of patients during flrst visit, with signiflcant decrease to 34.7% at the end of the intervention. Our data are in line with the literature, which has observed that 90% of palliative cancer patients have dry mouth[2,14]. This may be caused by the tumor itself, by inadequate hydration, by treatment with some drugs and by head and neck radiotherapy[3].

Dysgeusia, second most important complaint, was signiflcantly decreased between both visits, from 60.8% to 8.6%. This complaint is primarily a function of drugs such as tricyclic antidepressants, in addition to chemotherapy and radiotherapy, depending on tumor location[3].

In our study, candidiasis had satisfactory results after the intervention, decreasing from 43.4% to 14.0% ($p < 0.05$). Oral candidiasis is caused by the proliferation of candida species, especially *C. albicans*. Many deaths of cancer patients are caused by fungal sepsis, being 60% of cases related to pre-existing infections[14]. Oral candidiasis may be treated with local antifungal or systemic drugs[10].

In our study, chamomile tea has improved in‡ammatory symptoms; however no comparative study was carried out to determine the signiflcance of it to control mucositis symptoms.

Mouthwashes with chamomile tea, in spite of their unproven effect, seem to signiflcantly decrease and relieve major mucositis complaints, which may be associated to the anti-in‡ammatory action of this herb[13].

Oral mucositis treatment approaches include systemic analgesics, topic anesthetic or analgesic drugs[15].

Other factors may increase the incidence or worsen mucositis, such as alcohol and tobacco consumption. In our study, no patient used alcohol, however 30.4% were tobacco users, thus favoring taste changes, decreased food ingestion, dehydration and ineffective oral hygiene.

Some authors refer that, regardless of mucositis classifl-cation, oral hygiene is mandatory to decrease the in‡uence of oral bacterial ‡ora, pain symptoms and bleeding related to cancer therapy[3,11]. In general, smoker patients do not have adequate oral hygiene.

Our study has not observed correlation between oral complaints and the use of antibiotics. In spite of steroids instituted during flrst visit to control other symptoms, there has been no increased incidence of mucositis caused by this drug. Antibiotics may have direct effects on mouth or side-effects, as a consequence of their effects on accessory salivary glands, and steroids due to their immunosuppressive effects[11].

Although the therapy to treat mucositis had support and palliation characteristics, the intervention of the multidisciplinary team was more effective with regard to global attention, thus providing integral treatment to patients.

Simultaneous medical and nutritional treatment provides a better integration among professionals with regard to the choice of adequate drug therapy and diet-therapy for each patient, thus decreasing drugs potential adverse effects[2].

CONCLUSION

Oral mucositis is very common among cancer patients and a multiprofessional intervention is critical for the efflcient management of palliative care patients, respecting their autonomy and quality of life.

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