

# Management of hypopharyngeal mucositis in patients undergoing chemoradiotherapy in the head and neck region and its impact on swallowing: an integrative literature review

Impacto na deglutição e manejo da mucosite hipofaríngea em pacientes submetidos à quimiorradioterapia na região de cabeça e pescoço: uma revisão integrativa da literatura

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#### **ABSTRACT**

Purpose: To investigate the impact of chemoradiation-induced hypopharyngeal mucositis on swallowing and its management, based on an integrative literature review. Research strategy: Two researchers were responsible for the search and selection of articles, within the following databases: PubMed, Embase, Scopus, Science Direct, and Lilacs. Selection criteria: The search terms used were "Pharyngeal Mucositis", "Radiotherapy" and "Esophagitis", with the aid of the Boolean operator (AND). The search equation used was "Pharyngeal Mucositis" AND Radiotherapy AND Esophagitis. The following central question guided the study: "What is the assessment and management of radiation-induced hypopharyngeal mucositis in the head and neck region and its impact on swallowing?" Results: 75 studies were identified, of which 6 were excluded due to duplicity and 60 were excluded for not meeting the inclusion criteria; the remaining articles were read in full and 4 were selected to be part of the integrative literature review. Conclusion: Despite the scarce literature and little information on methods for evaluating hypopharyngeal mucositis, the articles point out that, regardless of the radiation dose, radiotherapy in the cervical region causes hypopharyngeal mucositis. Hypopharyngeal mucositis causes a great impact on swallowing, resulting in the need to use an alternative feeding route. In addition to the lack of information regarding the assessment and grading of hypopharyngeal mucositis, the studies do not discuss its direct treatment or prevention.

**Keywords:** Mucositis; Pharynx; Head and neck cancer; Swallowing disorders; Quality of life; Oral squamous cell carcinoma

#### **RESUMO**

Objetivo: Investigar o impacto da mucosite hipofaríngea quimiorradio induzida na deglutição e o seu manejo, a partir de uma revisão integrativa de literatura. Estratégia de pesquisa: A busca e a seleção dos artigos foram realizadas nas seguintes bases de dados: PubMed, Embase, Scopus, ScienceDirect e LILACS. Critérios de seleção: Os termos de busca utilizados foram "Pharyngeal Mucositis", "Radiotherapy" e "Esophagitis", com auxílio do operador booleano (AND). A equação de busca utilizada foi: "Pharyngeal Mucositis" AND "Radiotherapy" AND "Esophagitis". A seguinte questão central orientou o estudo: "Qual a forma de avaliação e manejo da mucosite hipofaríngea induzida pela radiação na região de cabeça e pescoço e seu impacto na deglutição?". Resultados: Foram identificados 75 estudos, sendo que 6 foram excluídos devido à duplicidade e 60 foram excluídos por não se encaixarem nos critérios de inclusão; os artigos restantes foram lidos na íntegra e 4 foram selecionados para fazerem parte desta revisão integrativa da literatura. Conclusão: Apesar da escassa literatura e das poucas informações sobre os métodos de avaliação da mucosite hipofaríngea, os artigos apontam que, independentemente da dose de radiação, a radioterapia na região cervical causa mucosite hipofaríngea. A mucosite hipofaríngea provoca grande impacto na deglutição, resultando na necessidade de uso de via alternativa de alimentação. Além da ausência de informações quanto à avaliação e graduação da mucosite hipofaríngea, os estudos não discutem o tratamento direto ou a prevenção desse tipo de doença.

Palavras-chave: Mucosite; Faringe; Câncer de cabeça e pescoço; Transtornos de deglutição; Qualidade de vida; Carcinoma de células escamosas

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## **INTRODUCTION**

Autonomous, excessive, and disordered growth of malignant cells, which can invade adjacent tissues and organs, is called cancer. Head and neck cancer (henceforth HNC) comprises a group of malignant tumors with different clinical presentations, which can affect the lips, oral cavity (buccal mucosa, gingiva, hard palate, tongue, and floor of the mouth), pharynx (oropharynx, nasopharynx, and hypopharynx), larynx, nasal cavity and thyroid<sup>(1)</sup>.

According to data from INCA, the Brazilian National Cancer Institute, cancers of the oral cavity and larynx are among the ten most common types of cancer in men in Brazil. The number of new cases of oral cavity cancer expected for Brazil, for each year of the triennium 2020-2022, will be 11,180 cases in men and 4,010 in women, corresponding to an estimated risk of 10.69 new cases per 100 thousand men and 3.71 for every 100 thousand women. Worldwide, more than 830,000 people are diagnosed with HNC and more than 430,000 patients die each year<sup>(2)</sup>.

Cancer can be defined as a multicausal chronic disease, being related to genetic and environmental factors. Smoking and alcohol consumption are identified as the main causes of HNC. Continuing tobacco use after starting treatment increases the risk of recurrence and the development of a second tumor. Approximately 20 to 50% of patients with oral cancer continue to smoke even after the end of cancer treatment<sup>(3)</sup>. Other factors are involved in the etiopathogenesis of Lip Cancer, such as occupational exposure to external carcinogens such as ultraviolet light. The increase in the incidence of cancer at the base of the tongue and tonsils has been justified by the high prevalence of some oncogenic subtypes of human papillomavirus (HPV) in the last decade<sup>(2)</sup>.

Treatment for HNC is complex and can be multimodal, depending on the lesion staging. Among the treatment options are (1) surgery to remove the tumor, (2) radiotherapy and (3) chemotherapy, depending on the possibility of performing the surgery, its location, and the feasibility of preserving the structures<sup>(4)</sup>.

Radiotherapy (RDT) is widely used as an adjuvant treatment to surgery and uses electromagnetic ionizing energy capable of causing chemical and biological effects that prevent the replication of neoplastic cells, inhibiting metastases and increasing patient survival. This treatment method can be used in combination with chemotherapy<sup>(5)</sup>.

As a result of RDT treatment, patients have adverse effects that represent a great impact on quality of life. Mucositis, xerostomia, dysphagia, skin reactions, among others, are some of the reactions found. Side effects are related to the total dose of RDT, daily dose, energy used, volume of irradiated area, type of technology and equipment used in irradiation<sup>(6)</sup>.

Radiation-induced hypopharyngeal mucositis is characterized as an inflammatory process, with erythematous and ulcerated areas, causing excruciation. This type of mucositis limits basic stomatognathic functions, such as chewing and swallowing, increasing the risk of malnutrition and dehydration, and directly impacting these patients' quality of life<sup>(7)</sup>.

It is noted that one of the most considerable discomforts of the acute reaction of RDT is odynophagia, that is, the pain to swallow, resulting from the inflammatory process also in the hypopharyngeal region. The literature is robust when it comes to the assessment and management of oral mucositis; however, few studies report the management of hypopharyngeal mucositis.

### **PURPOSE**

Taking into account the above-mentioned, the objective of this study was to identify the available literature on the impact and management of radiation-induced hypopharyngeal mucositis in the head and neck region, by means of an integrative literature review. This method provides a more comprehensive understanding of the studied phenomenon, allowing the combination of experimental and non-experimental studies<sup>(8)</sup>. In addition, the integrative review provides the incorporation of the applicability of results of significant studies in practice<sup>(9)</sup>.

This integrative literature review allowed the deepening of knowledge about hypopharyngeal mucositis, a topic rarely addressed in the national and international literature.

#### **RESEARCH STRATEGY**

The following central question guided the study: "What is the form of evaluation and management of radiation-induced hypopharyngeal mucositis in the head and neck region and its impact on swallowing?" The inclusion criteria were: original articles in their full version, without delimitation of year, in English, Portuguese or Spanish, that addressed the aspects of evaluation and management of hypopharyngeal mucositis. Duplicate papers, ordinances, editorials, opinion articles, as well as documents and abstracts of seminars, congresses, courses and those not available in their full versions were excluded.

## **SELECTION CRITERIA**

The search and selection of articles were performed in the following databases: PubMed, Embase, Scopus, ScienceDirect and LILACS (Latin American and Caribbean Literature on Health Sciences). The search terms used were "Pharyngeal Mucositis", "Radiotherapy" and "Esophagitis", with the aid of the Boolean operator (AND). The search equation used was: "Pharyngeal Mucositis" AND "Radiotherapy" AND "Esophagitis". The descriptors used for the search were selected from the search in DeCS (Descriptors in Health Sciences) and MeSH (Medical Subject Headings). It is worth mentioning that the term "Pharyngeal Mucositis", as it does not present robust literature on the subject, is not included in the medical metadata system; however, it was chosen to use it due to the absence of another term suitable for the search. Although this review aims at the theme of oropharyngeal mucositis, it was decided not to include this term, due to the high concentration of studies focusing only on oral mucositis, without studying the pharyngeal region.

After the survey of the publications, titles and abstracts were read, according to the inclusion and exclusion criteria. Then, the full articles were read to define and select the publications of the integrative literature review.

#### **RESULTS**

75 articles were identified, of which 6 were excluded by virtue of duplicity. After analyzing the titles and abstracts, 60 studies were also excluded for not meeting the inclusion criteria. The remaining articles were read in full and 4 of them were selected for the integrative literature review, as shown in Figure 1. The articles and their findings are described in Chart 1.

## **Main findings**

In the first study analyzed<sup>(10)</sup> all the patients received conventional fractionated radiation, with total doses ranging from 60-66 Gy to the tumor bed, 54-60 Gy to the pharyngeal axis, and 50 -54 Gy to prophylactically treated lymph node areas. Patients underwent adjuvant chemotherapy with cisplatin, weekly administered with a dose of 40 mg/m². Of the 40 patients in the sample, 36 of them underwent percutaneous gastrostomy before starting treatment; 34 of them left the alternative feeding route 6 months after the end of treatment. After treatment, 18 patients had esophageal strictures requiring dilation; 20 patients developed grade 2 xerostomia; 1 patient had trismus. The study did not present data on the method of evaluation and management of mucositis and esophagitis manifested in patients<sup>(10)</sup>.

In the second study, the patient's initial treatment was chemotherapy, with the use of Carboplatin and Paclitaxel, and RDT with a dose of 30Gy. After 5 cycles of chemotherapy, the treatment was changed to Crizotinib, but spinal and intramedullary metastases were identified in C4/5. The patient underwent RDT sessions in the regions from C3 to C5 with 30Gy in 10 fractions, concomitant with the use of Crizotinib<sup>(11)</sup>.

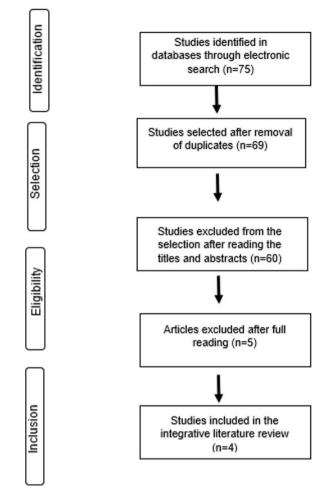


Figure 1. Organization chart of the process of search and selection of articles Source: Prepared by the authors, 2022

Chart 1. Publications that comprised the present study according to authorship, year of publication, title, objective, method, and main findings

Authorship/ Year	Title	Objective	Methodology	Main Findings
Eldeeb, H. et al.; 2012 <sup>(10)</sup>	Squamous cell carcinoma metastatic to cervical lymph nodes from unknown primary origin: The impact of chemoradiotherapy	Evaluate the impact of chemoradiotherapy in patients with metastatic squamous cell carcinoma for cervical lymph nodes	Retrospective Study	Most patients (75%) developed grade 3 mucositis, while only 11 patients (27.5%) had grade 3 or 4 dermatitis. 30 patients had grade 3 esophagitis. From these 40 patients, 36 underwent prophylactic gastrostomy placement prior to treatment
Zimmermann, MH. et al.; 2017 <sup>(11)</sup>	Hypopharyngeal and upper esophageal ulceration after cervical spine radiotherapy concurrent with Crizotinib	Describe upper hypopharyngeal and esophageal ulceration after use of Crizotinib	Case study	After 8 fractions of radiation, the patient developed increasing dysphagia. Ulceration of the hypopharynx and upper esophagus were evident on esophagoscopy, and CT. Hospitalization was required for analgesia and percutaneous endoscopic gastrostomy.
Brand, FZA. et al.; 2018 <sup>(12)</sup>	Severe immune mucositis and esophagitis in metastatic squamous carcinoma of the larynx associated with pembrolizumab	Describe the adverse effects of the use of Pembrolizumab in a 69-year-old patient	Case study	After 14 cycles of Pembrolizumab 200 mg, every 3 weeks, the patient presented dysphagia and grade 4 of oropharyngeal mucositis and ulcerative esophagitis. Pembrolizumab was discontinued and methylprednisolone 2 mg/kg/day was started, reducing to grade 1 oropharyngeal mucositis. Topical lidocaine was also used as part of the treatment.
Rath, S. et al.; 2019 <sup>(13)</sup>	Evaluation of purely accelerated six fractions per week radiotherapy in postoperative oral cavity squamous cell carcinoma	Assess the role of modestly accelerated pure and fractional radiotherapy using six fractions per week in postoperative patients of oral cavity squamous cell carcinoma	Interventional cohort study, prospective	Grade 3 oropharyngeal mucositis, pharyngeal/esophageal toxicity and skin toxicity were observed in 77,5%, 25% and 17,5%, respectively. Two patients had grade 4 mucositis. 47,5%

After 8 sessions of RDT, the patient reported increased dysphagia, was hospitalized, and started on exclusive parenteral nutrition. After two weeks, the patient required a percutaneous gastrostomy. The patient resumed oral feedings 3 weeks after symptom reduction and the percutaneous endoscopic gastrostomy was withdrawn after 6 weeks. The study did not address methods of managing radiation-induced pharyngeal and esophageal mucositis. The study concluded that the interaction between radiotherapy and the use of Crizotinib increases the risk of adverse effects, such as hypopharyngeal mucositis and esophageal ulcerations<sup>(11)</sup>.

In another case report, the patient underwent 3 cycles of chemotherapy with the use of cisplatin and associated RDT (66 Gy). Six months after the end of the adjuvant therapy, the patient presented multiple pulmonary nodules, thus initiating the use of Pembrolizumab<sup>(12)</sup>. After two weeks, the patient required hospitalization as a consequence of progressive dysphagia and consequent weight loss (6kg), referring to difficulties in ingesting liquids and solids due to ulcers in the oropharyngeal region. The patient underwent gastroscopy, which revealed severe esophageal ulcerations<sup>(12)</sup>. After 3 months, a new gastroscopy was performed, and incomplete healing of the pharyngoesophageal mucosa was observed. Imputable to dysphagia, the patient underwent gastrostomy<sup>(12)</sup>.

In the last study analyzed<sup>(13)</sup>, patients were submitted to a total dose of 60 Gy, using three-dimensional conformal RDT. Throughout the radiotherapy treatment, 3 patients had to interrupt the RDT sessions, 2 of them due to grade 4 oropharyngeal mucositis and one of them due to grade 3 pharyngeal toxicity. At the end of the fifth week, 33 patients had grade 3 or greater oropharyngeal mucositis; grade 4 mucositis was uncovered in two patients. Grade 3 pharyngeal and esophageal toxicity was diagnosed in 10 patients(13). The study cited that the average weight loss of patients was 4 kg. 29 of the 40 patients required an alternative feeding route, with a mean length of stay of 22 days from the start of RDT. All patients returned to the safe oral route approximately 4 weeks after completion of RDT<sup>(13)</sup>. The research did not describe the method of evaluating oropharyngeal mucositis and pharyngoesophageal toxicity. Likewise, it did not report the treatments and management of mucositis.

### **DISCUSSION**

The aim of this integrative literature review was to investigate the theme of hypopharyngeal mucositis in patients undergoing chemoradiotherapy in the head and neck region. The main question was to understand the forms of evaluation and management of this mucositis, as well as the impact caused in these patients' swallowing process.

Authors<sup>(14)</sup> recommended the use of the term *food mucositis* to describe the injuries caused by cancer therapies throughout the alimentary tract (from the mouth to the anus) because their mucous membranes have many similarities.

Radiation-induced oral mucositis is widely discussed in the literature. Its pathogenesis occurs, initially, by direct damage of cellular DNA, followed by tissue damage of the submucosa and basal layer of the epithelium, which leads to inflammation and ulceration of tissues in more severe cases. It is a common and frequent condition in patients with HNC undergoing chemoradiotherapy and can occur in up to 100% of them, causing a lot of pain and discomfort to different degrees<sup>(15)</sup>.

On the other hand, RDT-induced hypopharyngeal mucositis is little studied. Only 4 studies on this subject were identified, in which patients presented oral squamous cell carcinoma with metastasis in cervical lymph nodes<sup>(10)</sup>, lung adenocarcinoma<sup>(11)</sup>, laryngeal carcinoma of squamous cells<sup>(12)</sup> and another, also in the oral cavity<sup>(13)</sup>, and in all cases, as a form of treatment, they underwent chemotherapy and radiotherapy in the head and neck region. The RDT dose received by the patients in the studies ranged from 30Gy to 66Gy, with an average of 60Gy. Studies on the dose/effect of RDT on oral mucositis describe that the degree of severity of mucositis is closely related to the total radiation dose received by the patient, treated volume, fractionation, and treatment time<sup>(16)</sup>.

Patients with HNC receive a curative dose of around 50 to 70Gy, applied fractionally, once a day, 5 days a week, for 5 to 7 weeks. Studies already point to radiation toxicity effects from 10Gy. Patients submitted to conventional fractional RDT have 97% incidence of oral mucositis, this rate changes to 100% for those receiving accelerated or hyperfractionated fractionations, with an incidence of 47% of mucositis grades 3 and 4<sup>(17)</sup>.

The consequences of mucositis are devastating to the patient's health, and odynophagia and dysphagia are symptoms that commonly manifest and can imply malnutrition and dehydration, requiring, in many cases, the need for the use of an alternative feeding route. In cases where mucositis manifests more severely, hospitalization may be necessary on account of feeding difficulties and secondary infections. On top of that, for some patients, there is a need to reduce the chemotherapy dose and even discontinuation of RDT, directly interfering in the prognosis of the disease<sup>(18)</sup>.

In the present integrative review, the acute and/or chronic toxicity caused by RDT manifested in different forms and degrees. Among the manifestations found, we can mention oropharyngeal mucositis, hypopharyngeal mucositis, esophagitis, esophageal stenosis, xerostomia, trismus, dysphagia, and odynophagia. Only two studies described the methods used to define toxicity, using the radiation toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for the Treatment of Cancer<sup>(19)</sup>.

The incidence of dysphagia in patients receiving RDT in the head and neck region is high. More than 50% of patients with head and neck tumors have the symptom before even starting any treatment<sup>(20)</sup>. Among patients treated with RDT, a high percentage presents alterations in salivary and mucous glands, not to mention the conditions to the sensitivity and mobility of the oropharynx and larynx<sup>(21)</sup>.

Dysphagia was a common finding among the studies, appearing, on average, in the second week of radiotherapy treatment. It usually manifests severely, which can lead to hospitalization, weight loss, and the need for the use of alternative feeding routes; percutaneous gastrostomy is the most used route to meet the patients' nutritional demands. The time to withdraw from the alternative feeding route ranged from 4 weeks to 6 months. Only one study<sup>(13)</sup> cited the time between the beginning of RDT and placement of an alternative feeding route, with an average use of 22 days.

The damage around swallowing can also be attributed to RDT-induced fibrosis that would directly impact the musculature of the oropharynx, causing stiffness. Higher doses of radiation that include more constrictors of the pharynx lead to greater impairment in swallowing and airway protection.

Along with it, RDT can cause neuropathies that will affect the central areas in charge of swallowing<sup>(21)</sup>.

The authors of a study<sup>(20)</sup>, by means of a systematic review, compiled recent evidence and analyzed the relationship between RDT dose and the effects on the structures responsible for swallowing. The authors concluded that the average radiation dose in the constrictor muscles of the pharynx and larynx are the structures most frequently associated with dysphagia, especially when the dose is higher than 50Gy. Improvements in swallowing function were associated with lower dosage in the neck, upper constrictors of the pharynx, middle constrictors of the pharynx and esophageal intake.

In cases of dysphagia and odynophagia secondary to radiation-induced mucositis, the literature recommends early placement of alternative feeding pathways to reduce weight loss, avoid hospitalizations, and treatment discontinuation. Acute mucositis is dose-limiting of the chemotherapy treatment and is associated with long-term dysphagia<sup>(22)</sup>.

In all articles included in this study, patients underwent chemotherapy treatment associated with RDT. Chemotherapy treatment is aimed at the destruction of cancer cells, and the inhibition of cellular processes induces the appearance of mucositis lesions in the oral cavity. Authors<sup>(23)</sup> studied the severity of oral mucositis as an adverse effect of chemotherapy. The authors stated that the incidence of oral mucositis is varied, and that patients receiving Cisplatin, as an antineoplastic agent, had a more severe degree of mucositis, and oral toxicity was aggravated with the passage of chemotherapy cycles<sup>(23)</sup>.

The simultaneous use of radiotherapy and chemotherapy implies more severe and prolonged conditions of mucositis. The literature pointed out that chemotherapy-induced mucositis lasts for one week and resolution within 21 days after chemotherapy administration. The RDT-induced disease remains, at least, two weeks after the end of radiotherapy<sup>(24)</sup>.

In the present integrative literature review, only two articles described the way in which hypopharyngeal mucositis is evaluated and treated. In one of them<sup>(11)</sup> the patient underwent esophagoscopy, where deep ulcerated mucositis was detected in hypopharynx and inflammation of the upper 3cm of the esophagus, and management was carried out with the change of chemotherapy medication. As for the other study<sup>(12)</sup> physical examination and gastroscopy were performed, which revealed severe esophageal ulcerations, and oral prednisone associated with pantoprazole were used, in addition to the use of topical lidocaine, for the management of hypopharyngeal mucositis.

In the evaluation of oral mucositis, it is performed through oral inspection by a qualified professional, who will determine, by means of scales, the degree in which mucositis is found, defined using the Oral Toxicity Scale established by the World Health Organization (WHO)<sup>(25)</sup>. In the case of mucositis in a hypopharyngeal region, no consensus was found on its assessment and graduation of the level of involvement.

As far as the treatment and prevention of mucositis, there is no consensus in the literature in the matter of the use of protocols for both oral and hypopharyngeal mucositis. However, some studies address the use of topical and systemic therapies aimed at the management of oral mucositis<sup>(26)</sup>.

In 2020, the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology published the latest clinical practice guideline for the management of radiation-induced oral mucositis and chemotherapy<sup>(27)</sup> suggesting the implementation of oral care protocols combined with multiple agents for the prevention of oral mucositis.

Basic oral care should be maintained, including patient guidance, regular visits to the professional, and maintenance of oral hygiene and prostheses.

The use of toothbrushes with soft bristles, regularly changed, was also suggested, given the need to reduce aggression to the mucous membranes and maintain hygiene<sup>(28)</sup>. The guideline also suggested that the use of saltwater and sodium bicarbonate for mouthwashes did not have abundant evidence to be used in the prevention and treatment of oral mucositis. Nevertheless, their use could help maintain oral hygiene and patient comfort<sup>(28)</sup>.

In relation to mouthwashes, chlorhexidine was again cited as not suitable for use in patients performing RDT. Benzydamine was recommended in patients receiving low doses (<50Gy) of RDT, but further studies are needed for this evidence<sup>(28)</sup>, corroborating with the other research<sup>(29)</sup>. Mouthwash with vitamin E and vitamin A have also been shown to be effective in the treatment of oral mucositis<sup>(30)</sup>. Vitamin E has antioxidant properties and would eliminate free radicals released by inflammation; vitamin A would have an inhibiting effect on inflammation and epithelial proliferation<sup>(31)</sup>.

In the case of patients with mucositis suffering from severe painful symptomatology, authors<sup>(27)</sup> indicated the use of topical anesthetics for analgesia, such as mouthwash with 0.2% morphine as well as Doxepin in the management of oral mucositis pain in specific treatment sites. A randomized clinical trial<sup>(31)</sup> showed evidence in the use of benzocaine tablets – 25mg – to reduce soreness in oral mucositis and hypopharyngeal mucositis. Their results showed that pain after ingestion of a 25mg bupivacaine tablet was significantly lower in the 60-minute follow-up group compared to the control group.

Several lidocaine preparations, in the form of sprays or viscous solutions, are currently used for local anesthesia of the oral cavity and pharynx. These drugs have minimal systemic consequences and are great to be used in association<sup>(32)</sup>, but their effect would be fleeting, lasting from 15 to 30 minutes<sup>(33)</sup>. Other studies have reported that mouthwash of cold chamomile tea would cause relief from the painful symptoms of oral mucositis when performed several times a day. The anti-inflammatory potential of this herbal medicine<sup>(34)</sup>, which has flavonoids, inhibits the production of prostaglandins and the production of cyclooxygenase 2, resulting in the reduction of inflammation of oral mucositis<sup>(35)</sup>.

Authors<sup>(36)</sup> studied the efficacy of using low-cost therapeutic resources to relieve oral mucositis. The authors identified studies, which addressed the use of oral glutamine, honey and benzydamine, of these three resources, only oral glutamine presented evidence of improvement of oral mucositis, with reduction of the duration of oral mucositis, reduction of pain and a smaller number of participants required the use of alternative feeding route, agreeing with another study<sup>(37)</sup>.

Among the most explored therapeutic resources for the management of oral mucositis is photobiomodulation with Low-Level Laser Therapy. A randomized double-blind clinical study<sup>(38)</sup> investigated the efficacy of red and infrared lasers for the prevention and treatment of radiation-induced oral mucositis in patients with HNC. The authors concluded that the use of photobiomodulation is effective to prevent and treat oral mucositis in patients undergoing RDT, either associated with chemotherapy or not. The groups that associated the use of red and infrared lasers have better effects on oral mucositis.

As perceived through the results of this integrative review, there was no description of the treatment of mucositis in the hypopharyngeal region. The use of photobiomodulation has been described in the literature for the management of hypopharyngeal mucositis. The authors<sup>(39)</sup> researched the effect of using extraoral low-intensity laser, by means of the carotid trine protocol, which was defined through observation in cadavers, the region where the laser would reach the different tissues and cervical regions. Hypopharyngeal mucositis was determined from the report of patients' soreness in the region and odynophagia. It was possible to conclude that the laser of extra-oral use in the carotid trigone region promoted analgesia and comfort to the patients evaluated.

Authors<sup>(40)</sup> studied by means of a double-blind randomized clinical trial the safety and efficacy of the use of prophylactic extra-oral photobiomodulation for the prevention of oral diseases and oropharyngeal mucositis in patients with oral and oropharynx squamous cell carcinoma. The authors evaluated the degree of oral mucositis, pain level and patients' quality of life. The laser was applied to the face and neck in 5 different locations: right lateral face, central face in the lip area, left lateral face, cervical, left and right area. The study pointed out that patients who were part of the group that received photobiomodulation had lower severity and duration of oropharyngeal mucositis, with a longer symptom-free period compared to the placebo group. The placebo group presented higher pain scores and the need for analgesic and anti-inflammatory drugs, besides demonstrating worse performance in the quality-of-life questionnaire. The use of lasers was well tolerated by patients, with no significant adverse effects(40).

The importance of robust discussions and investigations about hypopharyngeal mucositis becomes fathomable when considering the increase in treatment costs with hospitalization, nutritional support, the need for medication use. Data are scarce when it comes to evaluation and management, directly impacting on the specificity of therapeutic approaches aimed at this group of patients, who need assertive interventions to reduce damage to quality of life.

# **CONCLUSION**

Notwithstanding the fact that there is no description of the way mucositis was directly evaluated, it was observed that, regardless of the radiation dose, radiotherapy in the cervical region resulted in mucositis in the hypopharyngeal region. Studies have shown that mucositis in this region had a great impact on swallowing, resulting in the need for the use of an alternative feeding route described in all studies. In addition to the lack of information regarding the evaluation and grading of hypopharyngeal mucositis, the studies are still initial and have not specifically reported on the direct treatment or prevention of this inflammatory process in this region.

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