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Oral Care of Pediatric Cancer Patients and the Use of Laser Therapy in the Treatment of Mucosites

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Abstract

Objective: to perform a literature review on the main oral manifestations and therapeutic possibilities in dentistry in pediatric cancer patients, highlighting laser therapy as the main form of treatment. **Material and methods:** the search were made in the Web of Science, PubMed and Cochrane Library databases, where articles from systematic reviews, meta-analysis and clinical trials published between 2009 and 2019 were selected. **Results:** we selected 41 articles that address the properties of low-intensity laser therapy in the treatment of pediatric cancer patients. **Conclusion:** studies show that low-level laser is clinically and functionally satisfactory and is especially effective in treating oral mucositis in pediatric patients undergoing oncotherapy, promoting an improvement in the quality of life of these patients.

Keywords: Medical oncology; Pediatric dentistry; Low-Level Light Therapy.

Introduction

Faced with radiotherapy and chemotherapy in the head and neck region, pediatric patients may present numerous complications in their oral cavity due to intense immunosuppression. Cancer treatment basically consists of surgery, radiotherapy and / or chemotherapy, depending on the type and stage of the tumor.[1,2]

The chances of chemotherapy treatment causing damage to the oral cavity increase according to the age of the patient. Overall, 40% of patients undergoing chemotherapy treatment develop oral changes, rising to over 90% when applied to children under 12 years. Although patients in this age group tend to develop malignant tumors that cause oral changes, it should be also considered that the high mitotic index of oral mucosa cells in this age group is a supporting factor. In addition, hematologic cancers, such as leukemia and lymphoma, may also be associated with a high frequency of oral complications as well as gastrointestinal tract neoplasms.[1-3]

Thus, the use of low level laser has been widely used in dental practices as a therapeutic treatment, with studies showing good results due to the acceleration of the healing process of lesions, through tissue biostimulation and promotion of pain relief. The possibilities of laser use have increased, and its use has been widespread in all different areas of medicine and dentistry, presenting itself as an excellent option for health care.[2-4]

The development of different types of lasers enabled the study for their use in various therapeutic and surgical procedures. Low level lasers have been developed for therapeutic use. Multiple other names have been given to these lasers, including soft laser, low reactivity laser, low energy laser, cold laser, and low intensity laser. Therapy with these lasers is often referred to as laser therapy.[5]

The aim of this literature review is to address the main oral manifestations affecting pediatric cancer patients, exposing the benefits of laser therapy as a treatment for these diseases.

Material and methods

For the preparation of this article, a research was conducted from September 2018 to June 2019, consulting the PubMed, Web of Science and Cochrane Library databases. Studies focusing on the treatment of oral lesions in pediatric cancer patients were sought, using a combination of the following descriptors: "pediatric dentistry", "oncology", "low intensity laser therapy", extracted from the Descriptors in Health Sciences (in Portuguese "Descritores em Ciências da Saúde" - DeCS) and Medical Subject Headings (MeSH). Scientific papers in English and Portuguese were selected when considered relevant, current and published in indexed journals, with the editorial board and ISSN (International Standard Serial Number). As inclusion criteria, publications from the years 2009 to 2019, published in Portuguese and English, were taken into consideration, bringing results from clinical trials, systematic reviews and meta-analyzes. Case reports and publications that did not have the full text available were excluded. After reading the titles and abstracts, duplicates were excluded, and 41 articles were selected due to the relation to the theme and relevance for the construction of this review.

Results

The studies selected in this review address the indications and benefits of laser therapy in pediatric cancer patients, contributing to professionals working with these patients to use this feature as an aid in the treatment of oral manifestations in this population.

It is necessary to discuss the main oral manifestations that can be evidenced in antineoplastic treatment in pediatric patients, highlighting the role of the dentist together with the medical team in the prevention, diagnosis, control and treatment of these changes in the oral cavity.

Childhood Cancer

Childhood cancer accounts for 2% to 3% of malignant neoplasms and has direct repercussions on quality of life. Its growth is relatively fast, with reduced latency period and possibility of being highly invasive. It is a group of various diseases that have uncontrolled abnormal cell proliferation in common and can affect any part or any organ of the body and is the second most common cause of death in children older than one year old.[6-8]

According to the National Cancer Institute of Brazil (2018), the most frequent tumors in childhood and adolescence are leukemias (affecting white blood cells), those of the central nervous system and lymphomas (lymphatic system). Also affecting children and adolescents there are other tumors, such as neuroblastoma (peripheral nervous system cell tumor, often abdominal), Wilms tumor (renal tumor type), retinoblastoma (affects the retina, the fundus), germ cell tumor (from cells that give rise to ovaries or testes), osteosarcoma (bone tumor) and sarcomas (soft tissue tumors).[9]

According to studies by Barbosa et al. (2010), one of the main resources used in childhood cancer treatment is chemotherapy alone or associated with surgery and radiotherapy. The main function of antineoplastic therapies is the destruction of malignant cells, preferably when they are in the mitosis phase.[9,10]

Thus, the younger the patient, the more likely chemotherapy will affect the oral cavity. About 40% of chemotherapy patients develop oral side effects. This number may be increased to over 90% in children under 12 years of age. As well as age, oral hygiene level before and during therapy, degree of malignancy, type and dosage of chemotherapy, and duration of chemotherapy are determinant factors for the severity of oral complications.[9-11]

In pediatric cancer patients, oral changes such as mucositis, candidiasis, xerostomia, gingival bleeding, and dysgeusia are common, which may have a direct impact on patients' daily activities, as well as being the focus for other infections.[1,9,10]

Frequent oral manifestations in pediatric cancer patients

Xerostomia

One of the frequent oral manifestations after radiotherapy, and in some cases after chemotherapy is xerostomia, being defined as a clinical condition that is characterized by quantitative and qualitative decrease in salivary flow. When in antineoplastic treatment, radiation is applied to the salivary glands, especially if the parotid is irradiated, saliva production tends to be compromised, becoming a transient change in salivary gland functioning, ceasing soon after its termination of treatment.[12,13]

Xerostomia influences both salivary factors and buffering capacity, increasing the enamel demineralization levels; in the amount of mucin, leaving the mucosa devoid of its protection against trauma and dehydration. There is also damage to its lubricating property, making it difficult to form and swallow the food bolus. Xerostomia also interferes with the phonation and retention of prostheses, besides bringing the sensation of burning mouth, difficulty eating, changes in taste sensitivity and halitosis.[12-15]

Regarding the treatment of xerostomia, some palliative measures are recommended to reduce the symptoms, such as the use of topical fluoride (in order to prevent cavities), artificial saliva, increased water intake and the use of sialogogues in order to improve the function of the saliva, reducing oral discomfort in the patient.[14,15]

Candidiasis

Among fungal infections, candidiasis is the most frequent, being an opportunistic infection caused by the fungus *Candida albicans*, common in babies and children. It usually presents with the following clinical forms: mucosal adherent white plaques, which are removable to scraping (pseudomembranous candidosis), red plaques associated with the loss of filiform papillae (candidiasis erythematosus), and white plaques that are not removed to scraping (chronic hyperplastic candidosis).[14,16]

Several factors contribute to the installation of infectious processes of fungal nature in patients with malignant neoplasms, such as myelosuppression, salivary flow impairment and mucosal injuries.[17]

Treatment of oral candidiasis may be systemic or local, through the use of antifungals such as ketoconazole and nystatin.[16-18]

Current studies recommend as a protocol for treatment of candidiasis in cancer patients the mouthwash with 5 mL of oral suspension of nystatin, five times a day for 15 days, requiring treatment to remain for another 7 days even after the disappearance of injuries.[14-17]

Taste disorders

According to Lopes and Nogueira (2012), the taste disorders caused by chemotherapy can be mild - hypogeusia - substantial loss of all four palates for a few weeks; or acute - dysgeusia - when there is persistent change in the sense of taste. This change usually disappears after a few weeks of discontinuation of treatment, but may be associated with

poor appetite, which leads to insufficient food intake and therefore weight loss during treatment.[19]

Chemotherapy promotes direct cytotoxicity to the papillae. The reestablishment of taste is quite variable among patients, perception may gradually normalize or become permanent in cases of severe xerostomia. The prevention and management of dysgeusia includes nutritional care, use of sodium bicarbonate oral rinse, frequent fluid intake, saliva substitutes, and prescription of zinc sulfate.[19,20]

Mucositis

Oral mucositis is considered an inflammation, and is accompanied by mucosal ulcerations, painful symptoms, with onset between 3 and 7 days after the start of chemotherapy and may last several days. Its first signs are marked by the presence of erythema in the buccal mucosa, soft palate, buccal floor and the ventral portion of the tongue, followed by edema and ulceration.[21,22]

Considered the most frequent direct toxicity in oral cavity, mucositis may occur due to the direct action of chemotherapy on oral mucosa cells or may be the result of myelosuppressive treatment, which leads to the occurrence of fungal, bacterial, viral and abnormal bleeding, leading neutropenic patients to a fourfold higher risk for systemic infection.[21-23]

Regarding its clinical aspects, there is a change in texture and differentiation in mucosal color, as well as epithelial atrophy, which may be presented as a symptom of mild to severe pain, according to the degree of tissue loss and aggression of pathogens. This change may progress to oral mucosal peeling, resulting in symptomatic ulcers, causing difficulty in speech and eating, with no available time for proper cell repair.[21,24]

Mucositis can present in four phases, as follow: *Inflammatory or vascular phase* (initial), occurring 24 to 36 hours after chemotherapy and / or radiotherapy. There is increased vascularization of epithelial cells and tissues due to the presence of cytokines such as interleukin 1 and tumor necrosis factor; *Epithelial phase*, occurring 4 to 5 days later, reducing cell turnover and causing tissue damage, atrophy and ulceration; *Ulcerative phase*, occurring after 1 week of drug administration, in which endotoxins progress the tissue damage, allowing opportunistic bacteria, viruses and fungi to proliferate; *Healing phase*, which begins 2 to 3 weeks, when cells and leukocytes begin being renewed. Healing is complete if there is no malnutrition and associated new opportunistic infections.[25]

The prevention and treatment of oral lesions resulting from antineoplastic treatment are fundamental, considering that oral mucositis seriously interferes in the prognosis of the patient, making them more susceptible to local and systemic infections, less tolerant to oral feeding, and may interfere on the dose and / or the chemotherapy drug used, prolonging the hospitalization time and, consequently, increasing the treatment costs.[24-26]

The treatment of mucositis can be performed with the combination of several therapies, however, it should be quick and effective, given the patient's morbidity during this pathological alteration. In children, treatment is usually conservatively performed, removing infectious foci prior to the start of chemotherapy, as well as using 0.12% chlorhexidine mouthwash as a chemical agent for an appropriate oral environment. Low-level laser therapy is currently indicated as a physical means of strengthening the epithelial layers, preventing recurrence and stimulating epithelial proliferation from the basal layer, as well as modulating action on the inflammatory response of the oral cavity.[27-29]

Laser therapy

Laser therapy in cancer patients with oral mucositis has known ability to provoke biological effects through photophysical and biochemical processes, increasing cellular metabolism. As it stimulates mitochondrial activity, the laser light acts as an anti-inflammatory, analgesic and healing of mucosal lesions. Thus, all energy emanating from the laser is absorbed by a thin layer of adjacent tissue and also absorbed at the point reached by radiation, triggering epithelial and fibroblast proliferation, as well as cellular and vascular changes. Collagen and elastin production, wound contraction, increased phagocytosis by macrophages, lymphocyte proliferation and activation, as well as tension force, accelerate healing.[30, 31]

The use of low-level laser therapy eliminates pain in the first application. This is believed to be due to the release of ßendorfin into the nerve endings of the ulcer, while promoting tissue biostimulation, leading the ulceration to repair within a faster time frame.[29-32]

In cases of mucositis, laser therapy provides pain relief, increased patient comfort, inflammation control, mucosal integrity maintenance, and better tissue repair.[33]

He-Ne (Helium-Neon) and GaAlAs (Gallium-Aluminum-Arsenic) lasers are the types with the best results for oral mucositis.[29]

The use of the He-Ne low-level laser (632.8nm, 60mW, 2J/cm2) applied daily before each radiotherapy session for seven weeks is a simple and non-traumatic technique for the prevention and treatment of mucositis of various origins, being able to reduce the severity and duration of oral mucositis associated with radiotherapy.[29,34,35]

Studies performed by Bensadoun et al. (1999) have shown a reduction in pain and an improvement in ingestion ability. The treatment is painless, little invasive (performed in the patient's oral cavity), low cost, and provides fast and safe application, with studies that prove its efficacy in the pro-

phylaxis and treatment of oral mucositis as well as of various other organic disorders.[34,35]

Therapeutic effects of laser therapy

The therapeutic properties of lasers have been studied since their discovery, and their analgesic action has been observed particularly on the forms of chronic pain of various etiopathogens, from peripheral receptors to central nervous system stimulation. Therefore, when laser light interacts with cells and tissue at the appropriate dose, certain cellular functions may be stimulated, such as lymphocyte stimulation, mast cell activation, increased mitochondrial ATP production, and proliferation of various types of cells.[36]

The analgesic effect of LLLT (low-level laser therapy) is due to the increased concentration of endorphin in cerebrospinal fluid. This endogenous peptide is considered a physiological analgesic factor that modulates central nervous system pain. It acts in the maintenance of the transmembrane potential, avoiding depolarization, by increasing the synthesis of ATP. This energy is used to expel Na^+ ions from inside the cell, making it difficult to transmit the local painful stimulus.[36]

The anti-inflammatory effect occurs through laser radiation, which promotes a significant increase in granulation mast cells, increasing the amount of histamine, which generates local circulatory changes such as vasodilation and increased vascular permeability, desirable in many situations.[36]

The antiedematous effect of LLLT results from stimulating microcirculation, providing better drainage conditions of extravasated plasma and fibrinolytic action, which provides effective resolution of the isolation caused by plasma coagulation.[36]

The biostimulation effect occurs when LLLT stimulates mitochondrial ATP production. LLL radiation also increases capillary neoformation and cell multiplication. Thus, the analgesic, anti-inflammatory, antiedematous and biostimulatory effects occur concomitantly on the treated area.[36]

Discussion

Currently, laser therapy has been used in several areas of dentistry due to its technology that provides greater comfort to patients and reliability to the professional.[14, 35, 36]

The studies by Albuquerque, Moraes and Sobral (2007) are in agreement with Cavalcante, Barros and Catão (2011) and Fiorentino et al. (2015), reiterating the advantages of using LLLT, which according to these authors provides relief of acute and chronic pain, promoting immediate and temporary analgesia; It may also be incorporated in the treatment of oral mucositis, herpes, aphthous lesions, candidiasis, neuralgia, xerostomia, facial palsy, joint pain, inflammation and lesions in the oral mucosa, dentinal hypersensitivity, temporomandibular disorders, periodontal disorders, restorative, orthodontic and endodontic treatments, post-surgical moment and headache.

Lasers can also be used as an antimicrobial, accelerating the repair and healing process of mucosal lesions.[29,34, 35, 36, 37]

The studies found in this review point to a correlation between cancer treatments and oral manifestations, in which the magnitude of these effects depend on a number of factors that are related to treatment, tumor and patient. The type and degree of tumor malignancy, the dose of the drugs administered, the duration of chemotherapy, the age and the level of oral hygiene before and during chemotherapy are determinant factors for the severity of oral complications, as chemotherapeutic agents act mainly on tumor cells, however, they may also cause damage mainly to tissues with rapid cellular proliferation, such as oral mucosa.[2-5,10,13]

Therefore, clinical and laboratory evidence has been accumulated supporting the use of LLLT. It has been effective in attempting to reduce the incidence of oral lesions and pain-associated factors in patients receiving high doses of chemotherapy and/or head and neck radiotherapy.[14,15,17,19,29,36,37]

Studies proposed by Barbosa, Ribeiro and Teixeira (2010) and Lopes, Nogueira and Lopes (2012) state that the younger the patient, the greater the likelihood of chemotherapy affecting the mouth. Thus, about 40% of these patients develop oral side effects, reinforcing the need to seek effective treatments and the need to include LLLT in these protocols.

Side effects in the mouth of children undergoing cancer treatment are much more common and more severe than in adult patients with the same condition. Studies suggest a probable increase in mitotic index of oral mucosa cells in this age group, being an adjuvant factor. Preventive measures such as topical use of 0.12% chlorhexidine gluconate, plaque and dental calculus removal, and intensification of oral hygiene care should be encouraged. In general, the oral pathologies found in pediatric cancer patients do not differ from those found in the general population. Many of these children are under 5 years old and have never received dental guidance or treatment. [22,39,40,41]

Conclusion

Oral manifestations are common in children undergoing antineoplastic treatment. Therefore, the presence of a dental surgeon in the multidisciplinary oncology team is of paramount importance in the follow-up of these patients, and may act in the prevention, early diagnosis and treatment of these manifestations. LLLT has been shown to be a very efficient and promising method for treating this condition, as it reduces pain and accelerates the healing process of these lesions, thus improving the quality of life of these patients.

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