

ISSN: 2230-9926

Available online at http://www.journalijdr.com



International Journal of Development Research Vol. 11, Issue, 02, pp. 44272-44275, February, 2021

https://doi.org/10.37118/ijdr.21021.02.2021



RESEARCH ARTICLE

OPEN ACCESS

DENTAL PERFORMANCE IN PREVENTION AND TREATMENT OF ORAL COMPLICATIONS IN CHILDREN AND ADOLESCENTS ONCOLOGICAL PATIENTS

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ARTICLE INFO

Article History:

Received 20th December, 2020 Received in revised form 14th December, 2020 Accepted 28th January, 2021 Published online 24th February, 2021

Key Words:

Pediatrics. Oral manifestations. Antineoplastic Protocols. Dentistry.

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ABSTRACT

Children and adolescents are at high risk of developing oral complications during and after chemotherapy and radiotherapy. The aim of this paper is discuss the main oral complications, dental management and the performance of the dentist before cancer treatment for children and adolescents. It is a literature review, which the descriptors "pediatrics", "oral manifestations" and "antineoplastic protocols" were used to search in the databases of MEDLINE/PubMED and SciELO. The most frequent oral complications in children and adolescents are: mucositis, candidiasis, glandular dysfunction, changes in taste and pain, in addition we can mention changes in craniofacial development. The patient must be instructed about oral hygiene and undergo dental treatment before the proposed treatments, in order to minimize oral complications. The dental protocol should also be extended during and after chemotherapy and radiotherapy in order to promote control of oral health and quality of life. The presence of a dentist in the multidisciplinary team is important to evaluate oral changes during cancer treatment.

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Citation: Alessandra Lais Pinho Valente Pires, Ana Letícia Marques de Souza Assis, Danilo Azevedo Campodonio Falcão, Lislândia de Jesus Mesquita, MarêssaCedraz de Oliveira, Pablo Carneiro de Oliveira Costa, Vanessa Oliveira Sousa Araújo, Victor da Silva Sampaio Lopes and Valéria Souza Freitaso, 2021. "Dental performance in prevention and treatment of oral complications in children and adolescents oncological patients", International Journal of Development Research, 11, (02), 44272-44275

INTRODUCTION

Cancer is part of a group of diseases that involve the uncontrolled growth of abnormal cells and can occur in any part of the body¹. In children and adolescents, it is considered rare, showing rapid growth and greater invasion capacity when compared to adult. It's an important cause of juvenile morbidity and mortality currently². The most common tumors at this age group are tumors of the central nervous system, leukemias and lymphomas. In relation to the head and neck region, the oral mucosa is the first site of greatest involvement, and sarcomas are the histological type most observed. Evidence points out that the incidence of oral and oropharyngeal cancer increased in adolescents due to infection with Human Papilloma Virus (HPV)^{3,4}. Regarding to the treatment of cancer in children and adolescents, it should be approached differently from adults, because of the difference between the primary tumor sites, the histological origin and their clinical behavior^{2,5}. Early diagnosis and evolution in treatment protocols have resulted in a progressive increase in the cure rates and a longer survival of these patients^{6,7}.

However, this progress comes through a higher incidence of adverse side effects in the face of the aggressiveness of the antineoplastic treatment⁸. Patients who have unfavorable oral health conditions such as dental infections, gingivitis and poor oral hygiene are at a higher risk of developing complications that may compromise systemic functions during the phases of immunosuppression induced by chemotherapy. While radiotherapy in the head and neck tends to potentiate these side effects⁹. In the field of dentistry, some measures before the beginning of cancer treatment can be established to balance the oral cavity, in order to minimize the side effects this treatment may cause, also possible systemic complications¹⁰. Therefore, the aim of this paper is to analyze the scientific production about the main oral complications of antineoplastic treatment and its dental management, as well as to highlight the importance of the performance of the dentist before the beginning of cancer treatment in children and adolescents.

MATERIAL AND METHODS

The present study is a review of literature based on the research of articles indexed in MEDLINE/PubMed and Scientific Electronic

Library Online (SciELO) databases, usingthecross-referencing of thefollowing descriptors in DeCs/MeSH in English and Portuguese: "pediatrics", "oral manifestations" and "antine oplastic protocols". To the inclusion criteria was used scientific articles published in full, in the form of literature review, systematic review, case reports and epidemiological studies that addressed the theme. The exclusion criteria were letters to the editor and to those who were presented in duplicate.

RESULTS

Cancer is considered a rare disease in children and adolescents (aged from 0 to 19 years old). It corresponds from 1% to 3% of malignant tumors worldwide and, at this age group, these tumors show, in general, short latency periods, aggressiveness and fast growth, however, they respond well to antineoplastic therapy and have a good prognosis¹¹. The most frequent tumors in children and adolescents are tumors of the central nervous system, leukemias and lymphomas. Among these, the most common type of childhood cancer is Acute Lymphocytic Leukemia (ALL). ALL constitutes about a third of childhood malignancies and its highest incidence is among children aged from 2 to 5 years-old, in a percentage of 70%. It is a disease derived from undifferentiated lymphoid cells (lymphoblasts) which are present in large number in the bone marrow, thymus and lymph nodes¹⁰. The most commonly reported signs and symptoms are fever, vomiting, weight loss, bleeding, generalized adenomegaly, pallo, and generalized bone pain, which also are common symptoms to other diseases. It directly influences the delay in diagnosis¹². The treatment of malignant tumors in children and adolescents consists of surgery, radiotherapy and/or chemotherapy and the treatment of choice will depend on the type and stage of the tumor. Cancer treatment causes several adverse effects, mainly in the oral and gastrointestinal mucosa, bone marrow and skin, as a result of its high degree of mitotic activity 13.

Chemotherapy, due to its antitumoral effect, destroys or delays the division of cells with accelerated proliferation, so it does not promote a distinction between neoplastic cells and normal cells with high mitotic activity. For example, the cells of the oral mucosa, so it makes this region susceptible to the appearance of lesions due to the difficulty of cell renewal caused by drugs¹⁰. It is used to treat approximately 70% of oncologic patients and, among these patients 40% develop oral manifestations, with an increasing number to over 90% in children under 12 years old1. Radiotherapy has been one of the most widely used treatment of neoplasms, it is used individually or in association with chemotherapy and surgery. As well as any therapeutic modality, radiotherapy also has side effects, due to hypocellularity and tissue hypoxia caused by radiation⁵. Treatment using chemotherapy and radiotherapy can cause toxicity in several organs, including the oral cavity, especially in children and adolescents. These changes may be local and immediate (direct toxicity) as occurs in cases of tumors in the head and neck treated with only radiotherapy, or they can be diffuse (indirect toxicity) in cases treated with chemotherapy and radiotherapy⁹. The direct and indirect toxicity of antineoplastic agents may cause pain, mucositis, difficulties in chewing and swallowing, glandular dysfunctions and changes in taste. These conditions can compromise the nutritional status of the patient, harms recovery, evolution of treatment and, often, causing delay in subsequent cycles of chemotherapy or radiotherapy sessions. The knowledge that some chemotherapeutic drugs cause greater toxicity to the oral mucosa allows preventive measures to be applied¹⁰.

Main oral complications of cancer treatment and dental management

Bleeding: Among all the complications, bleeding is the most predictable and preventable. Thus, the dentist must be informed about the patient's platelet count before any surgical intervention, because a count less than or equal to 75,000 platelets/mm³ facilitates a

hemorrhagic condition and any type of elective interventions in these cases should be avoided¹⁴.

Infection: One of the most common fungal infections in children and adolescents during oncologic treatment is Candidiasis. Several factors contribute to the installation and development of infectious processes by Candida species, including myelosuppression, salivary flow and mucosal lesions, as well as mucositis lesions. Oral candidiasis occurs frequently, but its episodes can be significantly reduced with the use of appropriate prophylactic measures¹⁵. According to Sena¹⁶, the treatment of fungal infections includes topical and systemic antifungal agents, in order to obtain greater efficiency in the fight against this infection. The most used are fluconazole and amphotericin B. Nystatin, ketoconazole, itraconazole and clotrimazole, are also used.

Xerostomia: Another frequent oral manifestation after radiotherapy and, sometimes, after chemotherapy, is xerostomia. This is defined as a clinical condition characterized by qualitative and quantitative reduction in salivary flow. When radiotherapy is applied to direct to the salivary glands, and especially if the parotid is included in the irradiated area, there is a reduction of saliva flow¹⁷. Xerostomia influences at some salivary factors, such as buffering capacity, which increases demineralization levels; amount of mucin, which leaves the mucosa without protection against trauma and dehydration; and its lubricating effect, making it difficult to form and swallow the bolus. Palliative measures are suggested to alleviate the symptoms of radio-induced xerostomia - such as the use of topical fluoride, to prevent cavities, artificial saliva, increase water intake and use of sialogogues - to improve salivary function and decrease mouth discomfort¹⁸.

Oral mucositis: Mucositis usually appears from 7 to 10 days during the treatment of chemotherapy and its severity depends on the aggressiveness of the drug, high doses and duration of the treatment. Mucosites are self-limiting when not complicated by other infections and usually disappear from 2 to 4 weeks after the cytotoxic effect of chemotherapy. The earliest manifestation in the oral mucosa is the appearance of a whitish color due to the lack of sufficient keratin flaking. This is followed by the loss of this layer and replacement by the atrophic mucosa, which is swollen, erythematous and friable. Subsequently, areas of ulceration appear with the formation of a yellowish and removable fibrinopurulent superficial membrane9. According to Fernandes⁵, pain, burning and discomfort are symptoms that can be intensified during alimentation or oral hygiene. The classification of the grading scales of mucositis according to the World Health Organization (WHO) is defined as: grade 0 - normal, intact mucosa; grade 1 - irritation, oral soreness and oral erythema; grade 2 - oral erythema, ulcer, solid diet tolerated; grade 3 - oral ulcers and liquid diet only; grade 4 - oral alimentation impossible. Studies have been done in some drug groups in order to determine which ones would be effective in preventing and/or treating this complication: vitamin E, anti-inflammatory agents, cytokines, prostaglandins E1 and E2, topical oral emollients, antioxidants, immunomodulatory drugs, antiviral drugs, antimicrobial agents and antiseptics. Most of these agents have not shown a significant favorable result, however some of them (such as prostaglandins) have not yet shown conclusive results, therefore further studies are needed¹⁹.

The symptomatic relief of patients with mild to moderate mucositis may be achieved by benzidamine hydrochloride. When it is more severe, a 2% lidocaine mouthwash can be used. Aspirin-mucin mouthwashes before meal may help to control dysphagia and prostaglandin has also showing a relief to this condition²⁰. Other treatment methods can also be of a great value in prevention/treatment. Cryotherapy causes local vasoconstriction, decreasing blood flow to the oral mucosa, thus reducing the damage to mucous cells, especially in chemotherapy. Low-level laser therapy accelerates tissue regeneration, decreasing inflammation and pain¹⁹. To prevent oral mucositis, it is necessary, one day after the end of chemotherapy, mouthwash with aluminum hydroxide 10% five times a day, for 7 days. After that, it should be reassessed the need to

continue the treatment. Laser therapy has also been used in the prevention and treatment of mucositis.

Radiation caries: Radiation caries usually appears from two months to one year after the beginning of radiotherapy treatment, characterized by being located around the cervical margins of the teeth. The entire dentition can be destroyed in a matter of months. The etiological factors are poor oral hygiene associated with a cariogenic diet¹⁸. When the change in diet is associated with the loss of buffer capacity of saliva and the difficulty of cleaning caused by pain in the mouth, there is an ideal environment for the development of dental caries, even on smooth surfaces or on cusp tips²¹.

Osteoradionecrosis: Osteoradionecrosis is a serious complication of radiotherapy in the head and neck. It is caused by a reduction of tissue vascularization. The consequent hypovascular and hypoxic conditions put at risk cell activity, collagen formation and wound healing capacity. When the vessels are altered, blood flow decreases, as well as nutrients and defense cells. Without nutrients and without defense the entire structure of the maxillary and mandibular bones undergoes degeneration². Bone necrosis is directly linked to radiation dosage, however the volume of irradiated bone and the proximity of the maximum radiation dose to the bone, have an effect on it. The risk of bone necrosis increases in the presence of teeth in poor condition, bone trauma, periodontal disease and when combined with chemotherapy. Exodontics, a known risk factor osteoradionecrosis, should be avoided after radiotherapy¹⁸. The treatment of osteoradionecrosis depends on its extent and is based on a combination of conservative measures and surgical resection. Among the conservative measures, the most used is topical or systemic antibiotic therapy. Local irrigation, hyperbaric oxygen therapy and, more recently, medicines derived from methylxanthines and antioxidants have also been used²².

Changes in craniofacial development: Radiotherapy leads to abnormalities of craniofacial development, such as maxillary and/or mandibular underdevelopment, formation of anomalous mineralized structures. Both chemotherapy and radiotherapy lead to changes in odontogenesis, enamel hypoplasia, dental organ development arrest, non-formation of teeth, microdontia, changes in rhizogenesis, such as interruption, tapering and enlargement of the pulp chamber. These effects are more pronounced when the two treatment are associated²³.

Dental performance in the prevention of oral complications that may occur during cancer treatment: The dental procedures should be performed as soon as possible, such as removal of destroyed teeth caused by caries or periodontal disease, deciduous teeth with physiological rhizolysis, teeth with pulp involvement, root rest and other procedures aimed at the adequacy of the oral environment before the cancer treatment. The ideal scenario for oncologic patients is to be examined by the dentist as soon as they have the disease diagnosed, the so that dental treatment precedes oncological treatment. These patients need priority in dental care to avoid delaying cancer treatment 10. The treatment of carious lesions must be carried out with the removal of all decayed tissue and the placement of ionomeric cements in order to adapt the oral environment. The presence of cavitated carious lesions represents a source of infection, a condition that can be aggravated due to xerostomia. The use of amalgam is contraindicated as a restorative material because it emits secondary radiation when the patient is submitted to radiotherapy in the head and neck, also for developing lichenoid reaction by contact involving the mucosa in contact with the dental amalgam². Patients with periodontal disease must undergo specific treatment, consisting of dental scaling and polishing. However, tooth extraction with periodontal pocket (>4mm) and/or grade I mobility should be performed. These, in addition to serving as a source of infection, could be complicated factors after radiotherapy, a period in which there are some limitations in the performance of extractions, due to the possibility to develop osteoradionecrosis²⁴. During chemotherapy, it is necessary to consult the oncologist whenever you need to perform any procedure, including prophylaxis; request a blood test from the oncologist 24 hours before any oral surgery or invasive procedures; always emphasize oral hygiene measures⁹. After therapy, the patient should be included in a periodic program of visits to the dentist considering the possibility of performing: oral examination, routine radiographs, oral hygiene instructions, elimination of infected teeth and dental prophylaxis¹⁰.

DISCUSSION

According to Machado², with the increase in survival and the decrease in the mortality rates of children and adolescents, the chances that they may have systemic changes resulting from the adverse effects of treatment, including oral manifestations, increase considerably, and may result in a worsening of the clinical picture with consequent worsening in the prognosis, given the increased risk of infections and increased length of hospital stay. Oncologic therapy causes damage to blood cells and immunosuppression. This fact results in a profile of patients susceptible to oral diseases that include mucositis, severe reductions in salivary flow, opportunistic infections by viruses and fungal, gingival changes, dysgeusia and dysphagia²⁵. Paiva²⁶, states that periodontal evaluation is important, especially when cancer treatment includes chemotherapy, since the risk of infection and bleeding increases considerably due to hematological changes. In addition, the loss of integrity of the gingival tissues, when combined with xerostomia, mucositis, changes in diet and poor oral hygiene, may cause oral problems, affecting the patient's quality of life, thus making it impossible to continue therapy. theassociationbetweensalivarydisorders, changes in microflora and myelosuppression, producedbycancertreatment, togingivalbleeding and patientdiscomfort. A previous adaptation of the oral environment of children and adolescents will significantly interfere with the quality of the patient's health during oncologic treatment. It is extremely important to have a dentist in the multidisciplinary team to provide better oral health, intervening when necessary and avoiding adverse effects during oncologic treatment²⁵.

Conclusion

Children and adolescents are particularly susceptible to the effects of antineoplastic treatment and, therefore, need special attention to prevent and treat these complications. The presence of the dentist in the multidisciplinary team is important to evaluate oral changes during cancer treatment.

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