Paediatric patients receiving oncology therapy: review of the literature and oral management guidelines

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ABSTRACT. Aim In recent years, neoplastic diseases in children have acquired growing importance in the field of paediatrics. This has been accompanied by significant advances in the treatment of children’s cancer, with long-term survival rates of 90% in the case of some tumors, resulting in the need for more medical and health care on all levels. With these advances comes a new responsibility to do everything possible to prevent complications stemming from neoplasia and its treatment. Among the side effects of cancer therapies (mainly chemotherapy and radiation treatment) are chronic or acute oral manifestations that are frequent sources of discomfort, focal points of systemic infections and other side effects, depending on the child’s stage of development. In most cases, the incidence and severity of oral complications are associated with preexisting factors (cavities, gum disease and poor hygiene) that clearly affect their emergence, increase and persistence. The aim of this article is to propose a guideline for managing oral complications of paediatric cancer treatments. Conclusions It is fundamental for the patient and their parents to be aware of the possibility of preventing or reducing problems in the oral cavity through preventive measures and simple oral treatment.

Keywords: Neoplasm, Mucositis, Xerostomia, Disgeusia, Osteoradionecrosis.

Introduction

Paediatric cancer occupies a small percentage among children’s illnesses as well as of the general population’s neoplastic diseases; however, it is the most frequent cause of death in children over the age of one, except for childhood accidents. The worldwide incidence is between 120 and 150 new cases per million for children under the age of 15, varying by age, sex, ethnicity and geographic location [Cabrerizo and Oñate, 2005].

Malignant tumors of the head and neck, including those of the central nervous system and the lymphatic system, accounts for 53% of childhood neoplasms. In addition, even if the tumor is located outside the maxillofacial area, the chemotherapy and radiation often required to treat the tumor have a strong potential for harming the orofacial structures [Da Fonseca, 2004; Goho, 1993; Rankin et al., 2003]. The child’s growth and development are seriously affected by the disease and by the treatment.

In recent decades the incidence of malignant tumors has increased, but there has been a global decrease in morbidity and mortality from these diseases, probably as a result of major diagnostic and therapeutic advances [Cabrerizo and Oñate, 2005]. The higher survival rate obliges us to prevent these side effects and improve the patients’ quality of life as much as possible.

Oral complications of chemotherapy and/or radiation in children

The epithelial cells of the oral mucous membranes are very sensitive to the effects of cancer therapy, because it inhibits the cell cycle, attacking the tissues with the greatest mitotic activity, which include tumors. But these patients are going through
a very active stage of odontogenesis, development and growth of dentition and craniofacial structures. For these reasons, oral complications in children with neoplasms are the result of the very defects of the neoplasia, the immunosuppressant potential of the therapies used, and their directly cytotoxic effect on the oral mucous membranes [Sepulveda et al., 2000].

**Dental, periodontal and bones changes**

Cancer treatment can severely alter odontogenesis. The younger the treated child is, the greater the oral complications, because both dentitions – deciduous and permanent – can be affected during the earlier stages of development [Cabrerizo and Oñate, 2005; National Cancer Institute, 2006] (Fig. 1).

In these patients, changes are common in tooth size (generally microdontia), number (generally agenesia), crown or root shape, root-crown correlation and mineralisation of the dental structure (Fig. 2). Delayed tooth eruption is also seen [Alpaslan et al., 1999; Antonadou et al., 2003; Cabrerizo and Oñate, 2005; Ferreti, 1990; Da Fonseca, 2004; Goho, 1993; Meraw and Reeve, 1998; National Cancer Institute, 2006; Simon and Roberts, 1991].

Dental caries and periodontal diseases are frequent in patients receiving radiotherapy of the head and neck (Fig. 3). Lowered immunity in these patients combined with inadequate oral hygiene may result in rapid destruction of dental and periodontal tissues [American Academy of Pediatric Dentistry, 2004-2005; Rankin et al., 2003].

In addition to severe changes in the dentition and gingiva, there is often a deficit in bone growth of the alveolar apophyses, where the dental roots are short, as well as in the maxilla and the mandible, due to damage in the growth centers. All this can affect the maturation of the craniofacial complex, causing asymmetrical facial growth and malocclusion [Rankin et al., 2003].

Whenever possible, lead or resin dental protectors, thick enough to prevent lesions, should be used.
Changes in buccal structures

Mucositis, inflammation of the mucous membranes, occurs due to the death of cells in the basal epithelial membrane. Clinical manifestations of mucositis generally begin during the second week of radiotherapy and last several weeks after treatment ends. The mucous membrane of the radiated area may remain thin and atrophic, and ulcerate with the slightest trauma, causing pain and considerable haemorrhaging, and increasing the risk of infection [Antonadou, 2003; Berg and Bleyer, 1995; Chen et al., 2004; Rankin et al., 2003; Simon and Roberts, 1991; Sonis, 2001].

Mucositis predisposes the colonisation of bacteria, fungi and virus reactivation, leading to opportunistic infections ranging from candidiasis, overgrowth of candida albicans, to septicemia [Antonadou, 2003; Berg and Bleyer, 1995; Chen et al., 2004; Childers, 1993; Simon and Roberts, 1991; Sepulveda, 2000; Sonis, 2001; Trotti, 2004]. These infections are promoted by changes in the oral microflora, as a consequence of the use of antibiotics and glucocorticoids, or in the presence of neutropenia [Chen et al., 2004; Da Fonseca 2004; Khan and Wingard, 2001; Rojas et al., 2001; Simon and Roberts, 1991; Trotti 2004].

Radiation of the salivary glands causes xerostomia, dry mouth, as a result of the atrophy of secretion cells and of the rest of the glandular cells [Ferreti, 1990; Rojas et al., 2001, 2005]. This is aggravated by the application of anticholinergic chemotherapy agents causing a severe decrease in the amount of saliva, lowered pH and remineralisation ability, and the appearance of dental caries caused by radiation, temporary hypogeusia and swallowing difficulties [Ferreti, 1990; Chen et al., 2004; Parliament et al., 2004; Rankin et al., 2003; Rojas et al., 2005].

Disgeusia, or loss of the sense of taste, occurs when the tongue is irradiated. It is generally temporary and the sense of taste is recovered after several months. However, if treatment affects the chemoreceptors on the back of the tongue, disgeusia may last for months or years [National Cancer Institute, 2006; Rankin et al., 2003].

Lockjaw, caused by contraction of the masticatory muscles, generally occurs 3-6 months after the conclusion of radiotherapy. The contractions are greater if the patient has undergone surgical resections and high doses of radiotherapy in the parotidean region and the masticatory muscles [American Academy of Pediatric Dentistry, 2004-2005; Meraw and Reeve, 1998; Rankin et al., 2003; National Cancer Institute, 2006].

It is important to stress that these alterations – i.e. mucositis, xerostomia and hypogeusia – often increase the possibility of a nutritional deficiency, which is the cause of alterations in dental development similar to those of rickets and malabsorption syndromes.

Considerations in dental treatment of children with cancer

The medical team of a child with cancer is multidisciplinary and should include a paediatric dentist from the start. It will be necessary to become familiar with the medical history and the data related to the tumor, the proposed palliative therapy or treatment plan, and pertinent information concerning the chemotherapy or radiotherapy, in order to prevent aftereffects and reduce the intensity of inevitable side effects. In addition, the team should be aware of the laboratory test data that could affect the dental treatments to be carried out [Rankin et al., 2003].

Paediatric dental treatment should be planned in conjunction with an analysis of the dental procedures’ systemic implications, the order in which they should...
be performed and management of the patient’s discomfort during dental treatments or to face possible oral complications as well [American Academy of Pediatric Dentistry 2004-2005; Rankin et al., 2003]. In general, the factors to be considered are the following.

- Whether or not to administer prophylactic antibiotics.
- The patient’s haematological status, to avoid certain dental treatments, or to administer specific systemic therapies prior to dental treatment, in order to prevent complications such as bleeding.
- The risk of opportunistic infections of the mouth, which could be a consequence of the cancer, inadequate oral hygiene, or excessive consumption of soft and sugar-laden foods. It should be emphasised that parents tend to overprotect children with cancer, and continue to do so after their children have overcome the disease [Méndez, 2005].
- The risk of neurotoxicity caused by the toxic effect of chemotherapy on peripheral nerves, leading to pain in the upper jaw or the mandible, or deep, intense and throbbing dental pain. The most revealing symptom is sleep disturbances [National Cancer Institute, 2006; Rankin et al., 2003].
- Complications stemming from osteoradionecrosis (ORN). Although infrequent in paediatric patients, oral management prior to treatment should concentrate on eliminating or reducing possible ORN focal points [American Academy of Pediatric Dentistry, 2004-2005; Meraw and Reeve, 1998; Parliament et al., 2004; Rojas et al., 2001]. In general, practitioners should avoid dental therapies with a risk of failure, based on the initial condition of the tooth or as a consequence of the cancer itself. The following assessment should be made: review the child health history; review current blood data; review the proposed chemotherapy/radiation protocol; complete a thorough head, neck and dental examination including panoramic and bitewing radiographs; give standard oral hygiene instruction and formulate a treatment in coordination with the patient, family and oncologist [Rankin et al., 2003].
- The need for intervention on the part of a psychologist or oncological psychologist, to deal with the disease’s emotional side effects, manifested in increased anxiety and fear of pain from any treatment. In conjunction with the rest of the multidisciplinary team, the psychologist should evaluate the hospitalised child’s emotional state and the risk of depression, which could make dental treatment more difficult [Méndez, 2005]. The need for psychotropic drugs to decrease anxiety should be evaluated.
- The importance of a dental health education programme aimed at the family, in order to maintain oral health and prevent complications from cancer treatment.

**Dental treatment: chronology**

Although these patients require continual evaluation of treatment and decisions, oral actions can be divided into three phases, in accordance with the patient’s medical status, cancer treatment and dental needs. Each treatment phase encompasses different problems and opportunities [Rankin et al., 2003].

- **Phase 1:** time period from the medical diagnosis until the start of chemotherapy and/or radiotherapy. The child’s cancer is active, resulting in haematological and systemic changes [Rankin et al., 2003].
- **Phase 2:** this period lasts approximately 30 to 45 days after the start of chemotherapy and/or radiotherapy [Rankin et al., 2003].
- **Phase 3:** after the conclusion of chemotherapy and/or radiotherapy, there is a long follow-up period lasting from one year to the patient’s whole lifetime [Rankin et al., 2003].

**Phase 1: management prior to chemotherapy and/or radiotherapy**

Proper management of a patient who is scheduled to receive cancer treatment requires the dental work to be completed 7 to 10 days before the start of chemotherapy/radiotherapy. Medical history, the degree of oral health and the prognosis of dental treatments are the variables to be considered [American Academy of Pediatric Dentistry, 2004-2005; Chen et al., 2004; Meraw and Reeve, 1998; Parliament et al., 2004; Rojas et al., 2001]. In general, practitioners should avoid dental therapies with a risk of failure, based on the initial condition of the tooth or as a consequence of the cancer itself. The following assessment should be made: review the child health history; review current blood data; review the proposed chemotherapy/radiation protocol; complete a thorough head, neck and dental examination including panoramic and bitewing radiographs; give standard oral hygiene instruction and formulate a treatment in coordination with the patient, family and oncologist [Rankin et al., 2003].

**Considerations regarding dental work**

Cavities should be filled. If the time available for dental treatment is short, the cavities at greatest risk, such as those which could affect the pulp, should be treated first. Fluoride therapy should be given in standard manner. Caries only involving the enamel should be restored, with temporary or definitive fillings depending of the period of time before therapy, in order to prevent them from worsening [American Academy of Pediatric Dentistry, 2004-2005; Cabrerizo and Oñate 2005; Rankin et al., 2003; Meraw and Reeve, 1998; National Cancer Institute, 2006].

If the dental pulp of permanent dentition but not the periapical region is affected, a pulpotomy or pulpectomy is indicated [Parliament et al., 2004;...
Dental surfaces or prostheses that may retain dental plaque or calculus should be smoothed [American Academy of Pediatric Dentistry, 2004-2005; Cabrerizo and Oñate, 2005; Meraw and Reeve, 1998; National Cancer Institute, 2006; Rankin et al., 2003]. The paediatric dentist applies a fluoride solution in gel or liquid form, to increase the dental surfaces’ resistance to attacks.

Before the start of active treatment, it is fundamental for the child to develop proper oral hygiene habits. This will prevent many complications and facilitate the treatment of any complications that will arise during chemotherapy and/or radiotherapy. It is the family’s responsibility to ensure proper oral hygiene because the child’s young age and poor physical condition prevent the child from doing so on his or her own.

The child and the family should remove dental plaque by brushing 2 or 3 times a day with a child’s soft toothbrush. After brushing, the child should rinse with a solution of either fluoride or chlorhexidine, as prescribed by the paediatric dentist [Barbería, 2005].

Phase 2: Management during chemotherapy and/or radiotherapy

Dental work should be completed before this phase, so that no dental pathology can risk complicating the child’s systemic condition even more. Likewise, the child’s oral health maintenance plan should be routine, and modified in accordance with the systemic changes reflected in lab results and the child’s general health.

During treatment, important systemic changes can result in opportunistic infections of the mouth and even septicemia, and platelet alterations can manifest themselves in bleeding gums, spontaneously as well as during brushing. Consequently, during this phase the oral health routine may be the following.

A. Brushing two or three times a day with a soft brush.

If the neutrophil count is less than 500/mm³ and the platelet count is less than 20,000/ mm³, the teeth should be cleaned with sterile gauze instead [Rankin et al., 2003].

B. Mouthwash rinses twice a day. If the child is under six years of age, or his or her physical condition makes it impossible to rinse, cotton balls or gauze soaked in mouthwash should be applied topically [Cabrera and Oñaite, 2005; Ferreti, 1990; Da Fonseca, 2004]. The products that have proved most useful in controlling bacterial plaque and dental demineralisation are a 0.05% fluoride solution and a 0.12% chlorhexidine solution, rinsed or applied for one minute just as long as the solution does not cause any secondary effects or allergies [Cabrera and Oñaite, 2005]. These products can be used alternately [Barbería, 2005].
The family should know that xerostomia associated with radiation therapy is generally permanent, so it will be important to use fluoride rinses throughout the patient’s lifetime [Rankin et al., 2003]. Studies on paediatric cancer patients support the use of a bicarbonate saline solution (0.9% sodium chloride and 5% sodium bicarbonate) after each meal, in the form of rinses or gauze soaked in the solution [Parliament et al., 2004; Rankin et al., 2003].

C. A balanced, non-cariogenic diet, avoiding an excess of mashed or blended foods. Parents and caregivers should be informed of the carbohydrate content of the foods and medications the child takes in, and encouraged to eliminate those foods that stay in the mouth for a long time [American Academy of Pediatric Dentistry, 2004-2005].

D. Prevention and treatment of opportunistic infections. Elimination of dental plaque and use of chlorhexidine solutions discussed in A and B will be sufficient to prevent some infections. In the case of an infection caused by Candida albicans, chlorhexidine should be replaced with nystatin, in gel or tablet form. It can be administered in combination with 200 mg of ketoconazole per day for 15 to 30 days [Khan and Wingard, 2001; Simon and Roberts, 1991]. If there is resistance to these pharmaceuticals, itraconazole can be administered [Khan and Wingard, 2001; National Cancer Institute, 2006; Rankin et al., 2003].

E. Prevention, as much as possible, of mucositis and lip lesions, avoiding the trauma that can be caused by excessively hard foods or excessively energetic brushing. Lip hydration products should be used to prevent dryness and cracking [American Academy of Pediatric Dentistry, 2004-2005; National Cancer Institute, 2006]. Mucositis can be treated with rinses, 3 to 4 times a day, with a solution of sodium bicarbonate, 2% viscous lidocaine, dyclonine hydrochloride, benzydamine hydrochloride, betacarotene and allopurinol; topical anaesthetics can be used to diminish local pain (3% xylocaine gel) [American Academy of Pediatric Dentistry, 2004-2005; Antonadou, 2003; Childers et al., 1993; Da Fonseca, 2004; National Cancer Institute, 2006; Parliament et al., 2004; Simon and Roberts, 1991].

F. Biopsy or dental treatments for eradication of sites of infection should be avoided. If they are indispensable, the oncologist should be consulted beforehand about the patient’s haematological status. Dental treatment should only be performed when platelet and neutrophil counts have recovered [American Academy of Pediatric Dentistry, 2004-2005; Rankin et al., 2003].

Phase 3: Management after chemotherapy and/or radiotherapy

As already mentioned, Phase 3 can last throughout the patient’s lifetime.

The younger the child is when the disease begins, the more medium- and long-term effects can be expected. In general, a schedule of check-up appointments can be set up every three months during the first year after completion of chemotherapy and radiotherapy, and every six months afterwards. These guidelines may be modified, depending on the oral health and other conditions found during each appointment.

Patients and their relatives should be encouraged to continue optimal oral hygiene and avoid cariogenic diet. They should be informed of the importance of this practice for the child’s overall health, and that it helps prevent orthodontic treatments, dental extractions and use of prostheses, whose success will be compromised for some time [American Academy of Pediatric Dentistry, 2004-2005; National Cancer Institute, 2006].

Conclusion

A high percentage of paediatric patients with malignant neoplasms have severe oral complications, and therefore the multidisciplinary treatment team of a child with cancer should include a paediatric dentist. When the cancer is diagnosed, the paediatric dentist should evaluate the patient’s oral health from two different perspectives.

The professional should detect any oral or dental lesions that could complicate the clinical treatment plan, to the point of threatening the patient’s life or needing an interruption or extension of cancer therapy, and should also try to prevent possible short-, medium- or long-term complications that could result from cancer therapy.

At the same time, dental professionals should team with the oncologist in order to provide prevention and/or the necessary oral treatments as soon as possible.

Within the multidisciplinary team, the paediatric dentist function is to carry out dental therapy prior to cancer treatment, design and implement the indicated oral health programmes needed in each case during the cancer treatment, and diagnose and treat any side effects.

It is important for the child to be included in the oral health care guidelines of the corresponding preventive dental unit, cooperating with the paediatric oncology unit.
References


