INTRODUCTION

Cancers of the head and neck region account for approximately 10% of malignant tumors worldwide. On average, 40% of such cases occur in the oral cavity, 25% occur in the larynx, 15% occur in the pharynx, 7% occur in salivary glands and 13% occur in other sites. Eight million new cases of cancer are reported every year throughout the world, over 200,000 of which originate in the oral cavity. The Brazilian INSTITUTO NACIONAL DO CÂNCER (INCA-BRASIL) estimated a total of 14,120 new cases of mouth cancer for 2010 (10,330 men and 3790 women) throughout Brazil and a total of 6214 individuals with mouth cancer died in the country in 2008 (4898 men and 1316 women).1-3

Head and neck radiotherapy and surgery are the most commonly employed treatments for combating this type of cancer. Patients submitted to radiotherapy of the head and neck often experience side effects and complications of stomatological interest. The most common complications are xerostomia, osteoradionecrosis, mucositis and candidiasis. Xerostomia is a dry mouth sensation that may or may not be caused by a reduction in salivary gland function, with alterations in the quantity and/or quality of the saliva. Osteoradionecrosis stems from ionizing radiation that affects the maxilla and/or mandible and is of considerable concern due to its aggressive nature. Mucositis is an inflammation of the oral mucosa that primarily affects radiotherapy patients and can cause peaks of intense pain. Candidiasis is the pathological emergence of lesions stemming from the development of Candida microorganisms.1,2,4

Dentists, oncologists and hearing/speech therapists should be aware of the oral complications stemming from radiotherapy in order to assist patients in obtaining a better quality of life during treatment for cancer.
METHOD

To carry out this study on oral health and radiation therapy for head and neck, we performed searches of scientific literature in the following databases / portals search: Pubmed / Medline, SciELO, LILACS, BIREME. The keywords and phrases used during searches in the databases were: oral health, head and neck radiotherapy, ionizing radiation, oral candidosis, radiotherapy, mucositis, xerostomia, osteoradionecrosis, salivary glands, hyposalivation. We used articles published in the last 10 years, corresponding to the period between 2000 and 2010, preferably in English, to provide relevance on the searched subject.

LITERATURE REVIEW

Head and neck radiotherapy

Radiotherapy is performed in an ionizing fashion. The extent of the lesion induced by radiotherapy depends on the malignancy and location of the tumor. The most important dose-limiting factor is the tolerance of the adjacent normal tissue. Tissues with a rapid return rate exhibit early effects, whereas those with a lesser return rate exhibit later onset effects. Accelerated fractionation is based on the observation that radiation causes accelerated proliferation of the tumor tissue, thereby diminishing the treatment time. Fractions are typically administrated twice per day. Hyperfractionation is a radiotherapy alternative employed to minimize side effects. This procedure makes use of the difference in repair capacity and tumor growth, as regulated by the fractioning of the dose. Thus, the conventional treatment time must be maintained with the administration of two fractions per day. With this type of fractionation, the total amount of the dose that the tumor absorbs can be increased as long as the healthy tissue is not compromised. Combinations of hyperfractionation and accelerated programs have proven successful for tumors that divide rapidly, but offer the disadvantage of having side effects, especially mucositis.

Three-dimensional therapy is a recent radiotherapeutic method in which high doses of radiation can be distributed spatially for a target volume, thereby reducing harm to normal tissue. However, further studies on this method are needed.

Xerostomia

Xerostomia (dry mouth) is one of the undesirable effects of head and neck radiotherapy. Saliva plays a fundamental role in the maintenance of homeostasis of the oral cavity and is one of the most complex, versatile and important fluids of the body, meeting a broad spectrum of physiological needs. The properties of saliva are essential to the protection of the oral cavity and gastrointestinal epithelium. Ninety percent of saliva is produced by the major salivary glands and the rest is produced by the salivary glands of the mucosa of the mouth and pharynx. The daily volume of saliva produced ranges from 0.5 to 1.5 liters and its pH oscillates between 6.5 and 7.4.

The following are the main functions of saliva: a) related to the liquid phase – cleaning of the oral cavity, clearing of food scraps and bacteria, solubilization of dietary substances contributing to sense of taste, lubrication of oral mucosa, facilitation of chewing, swallowing and speech; b) related to protection solutes of the teeth, neutralization of acids, participation in enamel formation, protection of oral mucosa and its coverage, defense from microorganisms and digestive action. It has also been suggested that the buffering system of saliva assists in controlling the effects of the reflux of gastric contents to the esophagus.

The effective reduction in the quantity of salivary flow is denomminated hyposalivation, whereas xerostomia is the subjective sensation of dry mouth, whether or not stemming from a reduction in the function of the salivary glands, with alterations in the quantity and/or quality of saliva. Xerostomy is a frequent symptom among patients under palliative care. Patients with no alteration in salivary flow may complain of dry mouth. Patients with xerostomia complain of oral discomfort, loss of the sense of taste and difficulty speaking and swallowing.

The extent of the lesion induced by radiotherapy depends on the volume of the irradiated glands (especially the parotid glands), the overall dose and the method employed. An acute phase of
xerostomia is commonly seen within the first week of radiotherapy, but there may be a late onset effect and permanent impairment of function. In other words, after some recovery, salivary secretion may subsequently regress in an irreversible manner. 2,12,14

Saliva also undergoes qualitative alterations stemming from radiotherapy, with a reduction in amylase activity, buffering capacity and pH, with consequent acidification. There are also alterations of different electrolytes, such as calcium, potassium, sodium and phosphate. Thus, individuals having undergone radiotherapy are more susceptible to periodontal disease and rampant caries as well as fungal and bacterial oral infections. Alterations produced in the salivary glands include acinose and adipose degeneration as well as fibrosis, with an accentuated reduction in salivary flow and an increase in the viscosity of saliva. Salivary secretion diminishes drastically when the salivary glands are included in the field of radiation. This reduction is related to the dose and duration of the radiation and reflects inflammatory and degenerative changes in the acini and cells in the ducts. In irradiated glands, the cell arrangement of the ducts is replaced by remaining loose, fibrous conjunctive tissue moderately infiltrated with lymphocytes and cellular plasma. 3,10,11-14

The treatment of xerostomia is essentially palliative. A direct relationship is described between the radiation dose and the extent of glandular changes. Xerostomia can be treated with mechanical/gustatory stimulants, saliva substitutes or systemic agents. Alternative methods, such as acupuncture, are also cited as a form of treating xerostomia. Saliva stimulants and substitutes generally only attenuate the xerostomia without altering salivary flow, whereas systemic agents attenuate xerostomia and also reduce the oral problems associated with hypofunction of the salivary glands by enhancing salivary flow. Therefore, the treatment of choice for xerostomia associated to radiotherapy is the use of systemic agents, among which pilocarpine is the most studied. Studies have shown that such systemic agents are more effective when used during radiotherapy. This was recently demonstrated for bethanechol, which, when used concomitantly to radiotherapy, has proven capable of increasing salivary flow at rest immediately after the end of radiotherapy and reducing the subjective complaint of dry mouth. 2,11,13,14

**Osteoradionecrosis**

Following radiation treatment, the tissue undergoes a number of alterations that turn it hypoxic, hypervascular and hypocellular, thereby impairing the reconstitution of bone and favoring the occurrence of osteoradionecrosis. Bone alterations are observed during procedures in the first year as well as the second and fifth year following radiotherapy, but there are reports of the occurrence of osteoradionecrosis three to seven months and 38 to 45 years after radiotherapy. 2,10,12,15-17

The clinical characteristics of osteoradionecrosis include ulceration of the mucosa with bone exposure and the presence of pain. The mandible is more affected than the maxilla. Diagnosis is based on both clinical and radiographic evaluation, with the presence of areas of resorption and bone neoformation. 2,4,12,15,18

Tooth extraction among patients having undergone radiotherapy is a concern due to the high risk of bone necrosis. For teeth indicated for extraction, the use of orthodontic elastics promotes avulsion through a less traumatic process. However, teeth that are strongly attached to the bone and have multiple roots are only removed by employing the conventional extraction method, for which hyperbaric oxygenation prior to and after the procedure is necessary in such cases. 3,12,16,19

A dental evaluation allows the determination of treatment needs prior to radiotherapy. This evaluation should include procedures such as the scraping of calculus, elimination of caries, orientation regarding oral hygiene and necessary extractions, thereby allowing the maintenance of oral health and the prevention of osteoradionecrosis. 2,15-19

**Mucositis**

Oral mucositis is the most common oral complication stemming from non-surgical cancer treatment and is characterized by painful, debilitating oral lesions. This condition is induced by cytotoxic drugs and radiation of the head and neck region. Mucositis occurs in 40% of patients receiving chemotherapy and 100% of those receiving head and neck radiotherapy. 2,4,10,20,22

The epithelial surface of the oral mucosa is in a constant process of cell renewal in which there is frequent cell loss due to mechanical trauma and compensated by the continual proliferation of cells in the basal layer. An imbalance between cell loss and proliferation leads to a reduction in epithelial cells, resulting in a thinner epithelium, which is manifested as mucositis in the oral mucosa. This proliferation occurs threefold more in children than adults. 20,22

Oral mucositis is classified as follows:

0 – absent (wet, pink mucosa and gums);
1 – whitish discoloration, enabling normal diet;
2 – erythema, enabling normal diet;
3 – pseudomembrane, requiring liquid diet;
4 – deep ulceration, rendering oral diet impossible. 2,12,20,23
The oral mucosa undergoes a series of changes related to the dose and duration of treatment. Edema and erythema are the first reactions to radiation due to vascular dilatation, with the mucosa intact and only a local burning sensation. The mucosa subsequently becomes stripped, ulcerated and covered with fibrinous exudate. Pain, burning and discomfort are commonly experienced while at rest and intensified by contact with hard and spicy foods. The involvement of the pharynx leads to difficulty swallowing and speaking. The tongue may exhibit atrophy of the papillae, inflammation, fissures, erosion and, in severe cases, areas of denudation. As the condition progresses, odynophagia, dysphagia and infection by opportunistic microorganisms may occur. Oral mucositis can also have a negative effect on adequate nutrition, leading to weight loss, anorexia, cachexia and dehydration and further restricting the patient to a liquid diet or even the indication of a nasogastric tube, which compromises overall health status. The perception of bitter and sour flavors is more affected than sweet and salty flavors. Patients attribute depression and sleep disorders to mucositis. It is necessary to control the symptoms, as adequate overall health status and nutrition affect a patient’s emotional state and immune system, making him/her more resistant to infection and the tumor itself.2,4,20,21

Patients should take special care with oral hygiene, such as brushing with a soft-bristle brush and fluoridated toothpaste, care with denture cleaning and adjustments, evaluation of the presence of caries, use of dental floss, adequate nutrition avoiding acid, spicy and sugary foods, and the maintenance of adequate hydration. Gargling with sodium bicarbonate creates an alkaline environment, which impedes the proliferation of candidiasis, but may have an unpleasant taste. Saline solution 0.9% is recommended, which is non-irritating and does not alter the pH of saliva. Despite the controversies, hydrogen peroxide is often used, but causes irritation and damage to granulation tissue, interrupts the normal flora of the oral cavity and the taste can cause nausea. Solutions with magnesium or aluminum hydroxide protect the mucosa by forming a layer with an analgesic effect and minimizing acidity, but dry out the oral mucosa and therefore require further research. Gargling with nystatin for the prevention of fungal infection is recommended three times a day for seven days prior to initiating treatment, as is gargling with sodium fluoride 0.05% (gel) daily. Chlorhexidine gluconate 0.12% is another recommended antimicrobial agent. Palifermin is a recombinant keratinocyte growth factor approved in Europe and the United States for reducing the incidence of oral mucositis in hematological malignancies. Moreover, a variety of alternative methods may be employed, such as distraction techniques, cognitive training programs, music therapy, massage and relaxation techniques, projection techniques, etc. Acupuncture has been considered, but requires further research.2,3,10,20,22,23

Periodic gargling with topical anesthetics containing lidocaine and benzylamine has been proposed. The administration of antibiotics has proven to be of some use in reducing the severity of radiation-induced mucositis. Topical doxepin has proven effective for severe mucositis in patients receiving radiation. A reduction in the inflammatory response stemming from radiotherapy can be achieved with the use of anti-inflammatory agents, such as pentoxifylline and indomethacin. In a number of studies, capsaicin, which is a potent inhibitor of neuropathic pain, has been demonstrated to reduce oral pain in patients with oral mucositis stemming from radiotherapy. Interleukin-11 inhibits pro-inflammatory factors, such as interleukin-12. 3,10,21,23

Low-level laser therapy has been used for the treatment and healing of oral mucositis, with positive results from the clinical and functional standpoint. Laser-irradiated cells lead to the release of growth factors by macrophages, the proliferation of keratinocytes, an increase in the population and degranulation of mastocytes and angiogenesis.2,20,23

**Candidiasis**

*Candida albicans* is the main etiological agent of oral candidiasis (thrush). The clinical manifestation of this condition is characterized by the presence of white deposits that are removed by scraping. Candidiasis may appear in pseudomembranous or erythematous form.2,3,10,24-26 Although a component of the normal oral flora, a number of factors may favor the growth of this opportunistic pathogen, which causes infection of the oral mucosa, vaginal mucosa or systemic illness. Patients undergoing head and neck radiotherapy experience a reduction in salivary flow, which may explain the increase in the occurrence of candidiasis. This condition is also generally associated with alterations in the sense of taste and mucositis.2,3,4,12,24-28

The diagnosis of candidiasis is performed though a clinical exam and treatment consists of the use of either topical or systemic antifungal agents, such as nystatin and fluconazole.3,10,25-27 The maintenance of oral health and regular dental follow up can prevent or considerably reduce the occurrence of candidiasis in patients undergoing head and neck radiotherapy.2,4,10,12,24-28

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CONCLUSION

Radiotherapy can have undesirable effects on the human organism, especially among patients submitted to head and neck radiotherapy. In such cases, oral complications are expected and dentists should provide orientation and intervention procedures in order to improve the quality of life of these patients.

REFERENCES


