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REVIEW ARTICLE

Dental extractions and radiotherapy in head and neck oncology: review of the literature

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Management of irradiated patients with cancer in the head and neck region represents a challenge for multidisciplinary teams. Radiotherapy promotes cellular and vascular decrease that results in a low response rate in the healing. Consequently, surgical procedures in irradiated tissues present high rates of complication. Osteoradionecrosis (ORN) is the most severe sequelae caused by radiotherapy. It is associated with previous extractions especially those carried out post-irradiation. The management of this side effect is difficult and can result in bone or soft tissue loss, affecting the quality of life. The literature regarding dental extractions performed before and after head and neck radiotherapy was evaluated, focusing on indications, criteria, surgical techniques and adjunctive therapies such as antibiotics and hyperbaric oxygen. Osteoradionecrosis can be minimized by oral evaluation and care prior to irradiation and healing time which allows tissue repair until the commencement of radiotherapy. In dental extractions realized after irradiation, minimal trauma, alveolectomy, primary alveolar closure and adjunctive therapies are recommended. Patients must be evaluated before radiation therapy and at that time all unrestorable teeth and/or teeth with periodontal problems must be extracted to reduce the post-radiotherapy exodontias that contribute to ORN. Once dental extractions become unavoidable after irradiation, additional care is needed.
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Introduction

Radiotherapy is largely used for treatment of head and neck cancer, as primary therapy, adjuvant to surgery, in conjunction with concurrent chemotherapy or as palliative treatment for late stage and unresectable head and neck malignancies. Although the radiotherapy can increase cure rates, the irradiated patient is susceptible to secondary effects that include mucositis, xerostomia, loss of taste, trismus, progressive periodontal attachment loss, dental caries (Figure 1), microvascular alteration, soft tissue necrosis and osteoradionecrosis (ORN) (Regezi *et al*, 1976; Sulaiman *et al*, 2003), this latter being considered the most severe sequelae (Lambert *et al*, 1997; Thorn *et al*, 2000; Kanatas *et al*, 2002; Sulaiman *et al*, 2003). The main causative factors of ORN (Figure 2) are bone biopsies, salvage surgery, trauma by prosthesis, dental or periodontal diseases, and extractions performed before and after radiotherapy (Beumer *et al*, 1983; Morrish *et al*, 1981; Epstein *et al*, 1987; Lambert *et al*, 1997; Vudiniabola *et al*, 1999; Oh *et al*, 2004).

Some potential complications following radiation therapy for head and neck cancer are unavoidable, mainly mucositis, loss of taste, xerostomia and microvascular alterations, but dental caries and ORN can be avoided by dental extractions of unrestorable tooth or those with advanced periodontal disease. However, the decision to extract tooth before or after radiotherapy has traditionally been based on clinical experience and empirically designed protocols. The literature data regarding dental evaluation and extraction are confusing and indeterminate, showing conflicting results when comparing extractions before and after radiation therapy (Starcke and Shannon, 1977; Beumer and Seto, 1981; Beumer *et al*, 1983; Sulaiman *et al*, 2003).

Extractions and radiotherapy

Unrepairable teeth due to caries, periodontal disease or root lesions can cause infection of the bone and progression to ORN because of low vascular patency and the inability of the mechanisms of repair in irradiated tissues (Costantino *et al*, 1995; Oh *et al*, 2004). The irradiated patients present alterations in the salivary glands and in the dental structure, which predispose to progressive periodontal attachment loss, rampant caries and fungal and bacterial infections.

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Figure 1 Multiple caries affecting the cervical region of the lower teeth in an irradiated patient

Figure 2 Mandibular osteoradionecrosis caused by tooth extraction after radiotherapy

These patients can also present fibrosis, resulting in trismus and consequently difficulties in adequate oral care (Chavez and Adkinson, 2001). For these reasons, non-collaborative patients, or those presenting decayed and non-restorable teeth, periodontally compromised teeth both partially erupted or without antagonist tooth, must receive exodontias before radiation therapy.

Knowledge of radiation dose, volume, modality, urgency, general state and prognosis plays an important role in the decision of teeth removal (Beumer and Seto, 1981; Sulaiman *et al*, 2003). Morrish *et al* (1981) studied 100 patients and observed 22 cases of ORN; all of them had been irradiated with doses over 6500 cGy. Thorn *et al* (2000) evaluated 80 cases of ORN and observed that in 93% of these cases the radiation doses were >6400 cGy. The authors concluded that patients who receive high doses of radiation therapy should be submitted to dental extractions of all unrestorable teeth before radiotherapy. Analysis of the field of radiation avoids unnecessary procedures, as extractions performed outside the area of radiation do not constitute a risk factor to the development of ORN (Sulaiman *et al*, 2003). These authors found statistical significance in the frequency of ORN when comparing teeth within and outside irradiation fields. Tumor prognosis is subjectively weighted as a priority in the decision-making. Extractions of unrestorable, but asymptomatic teeth in pre-radiation visits or in the post-radiation period in patients with advanced or end-stage diseases, are not advocated.

The irradiated tissues present low reparative ability and a major risk for ORN occurrence after surgical procedures compared to those in non-irradiated areas. However, the literature shows indeterminate results about exodontias performed before and after irradiation or in both. Most authors have demonstrated higher rates of ORN when teeth are removed after radiotherapy (Horiot *et al*, 1981; Morrish *et al*, 1983; Marx and Johnson, 1987; Thorn *et al*, 2000), but few studies have shown increased risk for ORN development when exodontias were executed before radiation treatment (Regezi *et al*, 1976; Sulaiman *et al*, 2003) and others show similar results when dental extractions were compared before and after radiotherapy (Epstein *et al*, 1987; Reuther *et al*, 2003). Horiot *et al* (1981) obtained 0% and 4.5% ORN rates after extractions in non-irradiated and irradiated fields, respectively. Morrish *et al* (1983) evaluated 100 irradiated patients and observed 22 cases of ORN, with 11 related to extractions performed within and three to extractions performed outside irradiation areas. Epstein *et al* (1987) observed 5.4% and 7.1% ORN rates after extractions in non-irradiated and irradiated fields, respectively. Marx and Johnson (1987) analyzed 536 cases of ORN, with 274 related to dental extractions. Of these, 207 occurred in association with teeth removal after, 57 before and 10 during radiation treatment. In 80 cases of ORN Thorn *et al* (2000) attributed 36 (45%) to extractions after radiotherapy and 8 (10%) to extractions before radiotherapy. In 2003, Reuther *et al* studied 68 cases of ORN in 830 irradiated patients, 16 (24%) out of 68 ORN cases being related to exodontias previously and 18 (26%) to extractions after radiotherapy. Inversely, there are studies that show higher ORN rates associated with extractions performed before radiotherapy. Regezi *et al* (1976) found 2% *vs* 0% after 311 dental extractions performed in 49 patients before irradiation and 23 extractions in 10 irradiated patients, respectively. Sulaiman *et al* (2003) evaluated 77 patients prior to radiotherapy with 197 teeth being extracted, and 107 irradiated patients in which were performed 330 exodontias. The authors found 2.6% and 1.8% of the ORN in non-irradiated and irradiated sites, respectively. Although there is a risk of ORN development related to dental extractions in irradiated fields, often these procedures are unavoidable because of dental infections. Usually, these exodontias are indicated due to fault or absence of previous radiotherapy evaluation by dentist and patient collaboration after oncological treatment.

Despite the conflicting results and discussion about 330 the most appropriate moment for extractions, there is growing consensus that multidisciplinary teams can reduce the irradiation sequelae and that it is also mandatory that before radiation therapy for head and neck cancer all patients undergo meticulous dental evaluation and rigorous follow-up during and after radiotherapy (Horiot *et al*, 1981; Morrish *et al*, 1981; Epstein *et al*, 1987; Makkonen *et al*, 1987; Marx and Johnson, 1987; Brown *et al*, 1990; Lambert *et al*, 1997; Tong *et al*, 1999; Reuther *et al*, 2003). Brown *et al* (1990) evaluated 92 patients and observed that 48 of these patients needed one or more extractions and all of them needed dental care before radiation treatment. They detailed that none of the evaluated patients developed ORN and stated the importance of adequate oral care before radiotherapy as discussed by Sulaiman *et al* (2003) who emphasized prior evaluation and follow-up as being responsible for low ORN rates (2.1%).

An important point when considering dental extractions before radiotherapy is the time interval between dental extractions and the beginning of radiation therapy. This time must be sufficient for initial healing and to allow that tissues support radiation delivered; however, the repairing time should not be extended for a long period that compromises oncologic treatment and prognosis (Starcke and Shannon, 1977; Beumer and Seto, 1981; Horiot *et al*, 1981; Beumer *et al*, 1983; Epstein *et al*, 1987; Marx and Johnson, 1987; Maxymiw *et al*, 1991; Costantino *et al*, 1995; Tong *et al*, 1999; Reuther *et al*, 2003). Regezi *et al* (1976) found only one case of ORN in 311 extractions performed in 49 patients between 10 and 14 days before radiotherapy. This healing period was similar to that recommended by Beumer *et al* (1983) who evaluated 120 individuals and found 13 episodes of ORN. Starcke and Shannon (1977) studied 62 patients, where 515 teeth were removed with a median of 25.3 days before radiotherapy. Only one patient presented ORN occurring spontaneously. Epstein *et al* (1987) presented five cases of ORN in 92 patients with 454 teeth extracted in a median of 26 days before commencement of radiotherapy. In the series of Sulaiman *et al* (2003), the patients had teeth removed in a median of 26.2 days before commencement of irradiation therapy. Only two cases of ORN (2.6%) were associated with this group. Oh *et al* (2004) studied 81 irradiated patients submitted to 99 third molars' extractions pre- and 7 third molars' extractions post-radiotherapy. There was only one case of ORN related to tooth extraction. The median time between extractions and irradiation was 32.4 days.

A wound due to surgical procedure (dental extraction) requires protein syntheses that are obtained by cellular activity and vascular events. (Marx *et al*, 1985; Maxymiw *et al*, 1991). Ionizing radiation promotes irreversible cellular and vascular damage resulting in hypoxic, hypocellular and hypovascular tissue. This fact can drastically affect the reparation process and there is a consensus that extractions in irradiated fields must be executed with as little trauma as possible. Minimal trauma, alveolectomy with careful bone trimming, conservative flaps, primary closure without tension and removal of few teeth per session minimize postoperative complications and are associated with lower ORN rates (Starcke and Shannon, 1977; Beumer and Seto, 1981; Horiot *et al*, 1981; Beumer *et al*, 1983; Marx *et al*, 1985; Epstein *et al*, 1987; Makkonen *et al*, 1987; Maxymiw *et al*, 1991; Lambert *et al*, 1997; Tong *et al*, 1999; Sulaiman *et al*, 2003; Oh *et al*, 2004). In an attempt to increase healing after exodontias or to avoid secondary infections, hyperbaric oxygenation (HBO) and prophylactic antibiotics have been used as adjuvant therapies in the surgical management of irradiated patients.

Adjunctive therapies

The use of HBO is well established in the treatment of ORN and has been employed as an adjuvant in extractions after radiotherapy (Marx *et al*, 1985; Costantino *et al*, 1995; Tong *et al*, 1999; Vudiniabola *et al*., 1999; Chavez and Adkinson, 2001). It increases tension and diffusion of oxygen in the irradiated tissues, collagen synthesis, vascular networking and metabolism of bone and consequently the healing of tissue (Marx *et al*, 1985; Lambert *et al*, 1997; Chavez and Adkinson, 2001). Marx and Johnson (1987) evaluated the effect of HBO on irradiated tissues of 50 patients and observed an increase in the number of fibroblasts and functionality of capillaries. Thorn *et al* (1997) compared transmucosal oxygen tensions of 10 patients irradiated with doses ranging from 6400 to 6600 cGy that developed ORN, and five non-irradiated individuals used as controls. The evaluations were performed before and after HBO. The control group presented median levels of oxygen of 40.5 mmHg (range 39.8–41.2 mmHg) and irradiated patients presented median of 20.4 mmHg (range 16.6–23.2 mmHg) before HBO. After HBO the irradiated patients presented median levels of transmucosal oxygen tension of 34.7 mmHg (range 27.8–40.0 mmHg), demonstrating the increasing in oxygen levels in irradiated tissues promoted by OHB. It pointed to an increasing reparation of the irradiated tissues.

Oxygen is inspired under pressure by individual (one-person) or multiplace hyperbaric chambers. The protocols usually consist of 20–30 dives before and 10 after tooth removal, with humidified pure oxygen administered at 2.4 atmospheres absolute pressure for 90–120 min each session, once a day (Marx *et al*, 1985; Lambert *et al*, 1997; Thorn *et al*, 1997; Chavez and Adkinson, 2001; Reuther *et al*, 2003; Sulaiman *et al*, 2003). Serious effects resulting from HBO are rare. Toxic effects are usually observed in the central nervous system and the main contraindications against the employment of HBO are some drugs, non-treated pneumothorax, neuritis, some forms of pulmonary disease, and active viral infections (Vudiniabola *et al*., 1999).

Another adjuvant that has been used in post-radiation extractions is the use of antibiotics, however, there is no consensus about their employment (Beumer and Seto,

1981; Makkonen *et al*, 1987; Costantino *et al*, 1995). The literature recommends antibiotics for exodontias associated with radiotherapy, especially in patients with risk of developing ORN. In general, the authors (Horiot *et al*, 1981; Beumer *et al*, 1983; Epstein *et al*, 1987; Makkonen *et al*, 1987; Maxymiw *et al*, 1991; Costatino *et al*, 1995; Tong *et al*, 1999; Kanatas *et al*, 2002; Sulaiman *et al*, 2003) comment briefly on the general use of antibiotics without details about its type, posology, and time. Kanatas *et al* (2002) conducted a study in consultation with the heads of oral and maxillofacial surgery departments about the use of antibiotics in dental extractions related to radiotherapy. Of the 79 answered questionnaires, 86% of the professionals recommended prophylactic antibiotics and 89% recommended therapeutic use for a hypothetical extraction of a mandibular residual root in irradiated fields, and OHB was recommended by 34%. The study of Maxymiw *et al* (1991) supports the use of antibiotics in extractions performed in irradiated sites. Antibiotics were prescribed prophylactically to 72 patients irradiated with median doses of 5000 cGy (range 2500–8400 cGy). In 196 extractions without HBO there were no cases of ORN.

Marx *et al* (1985) performed a randomized prospective study comparing HBO and antibiotics. The authors compared 137 dental extractions in 37 irradiated patients that received prophylactic antibiotics to 156 dental extractions in irradiated fields of 37 patients that received adjuvant HBO. All cases received doses >6000 cGy. The HBO protocol consisted of 20 sessions before the surgery and 10 sessions after surgery, each session lasting 90 min. Patients received 100% humidified oxygen at 2.4 atm. The antibiotic group received 1 000 000 U of aqueous G penicillin before extractions and 500 mg of fenoximetilpenicilin four times a day for 10 days after surgery. ORN occurred in 11 patients (29.9%) in the antibiotics group and in two patients (5.4%) in the HBO group. This paper has been considered the 'conclusive study' to date on why HBO should be considered and prescribed routinely for extractions in the irradiated sites. However, the authors have not detailed the degree of difficulty associated with teeth extraction and randomization process. Lambert *et al* (1997) employed the same protocol described by Marx *et al* (1985) and followed up 47 patients who had undergone dental extractions in irradiated fields (dose range 4500–7440 cGy) and did not find any cases of ORN. Tong *et al* (1999) concluded that antibiotics were not sufficient in reducing the risk of ORN development. In a study performed with 237 dental extractions in irradiated fields of 43 individuals that received doses ranging from 6000 to 11 250 cGy and prophylactic and therapeutic antibiotics for 7 days or while healing was not achieved, the authors observed delayed wounding of extracted tooth in nine patients (6.3%) and four cases of ORN (9.3%). Vudiniabola *et al*. (1999) studying 29 irradiated patients with doses ranging from 5000 to 6600 cGy who underwent adjuvant HBO and seven irradiated controls that did not receive hyperbaric oxygen found ORN rates of 4% in the HBO group and 15% in the control group. In 2001, Chavez and Adkinson studied 371 dental extractions in 40 patients that received median irradiation doses of 6200 cGy. The authors applied the same HBO protocol described by Marx *et al* (1985) and observed complete healing in 98.5% of dental alveolus. Annane *et al* (2004) conducted a multicentric, double-blind, placebo-controlled trial at 12 university hospitals in patients presenting ORN. The authors compared 31 patients that received 30 HBO sessions preoperatively and 10 postoperatively at 2.4 atm for 90 min, and 37 patients that received a placebo containing 9% oxygen and 91% nitrogen. They observed that after 1 year, 6 (19%) out of 31 patients in the HBO group and 12 (32%) out of 37 in the placebo arm had complete healing. The authors concluded that patients with mandibular ORN did not benefit from HBO.

In general, HBO and antibiotics have been considered favorable when used as adjuvants in dental extractions after radiotherapy, contributing to a low frequency of complications.

Conclusion

Before making the decision to extract teeth before or after radiotherapy, the individual characteristics of the patients, tumor and oncological treatment must be considered. Oral evaluation before radiotherapy reduces the risk of complications and dental extractions should preferably be performed before commencement of irradiation. For that reason, a multidisciplinary team consisting of the radiotherapist, oral and maxillofacial surgeon, head and neck surgeon, and oncologist is mandatory. Once dental extractions become unavoidable after radiotherapy they can be performed by specialists with appropriated surgical techniques, adjuvant therapies and rigorous follow-up after the surgical procedures.

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