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British Journal of Oral and Maxillofacial Surgery 54 (2016) 547–550

BRITISH Journal of Oral and Maxillofacial Surgery

www.bjoms.com

Prophylactic use of pentoxifylline and tocopherol in patients who require dental extractions after radiotherapy for cancer of the head and neck

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Accepted 18 February 2016
Available online 11 March 2016

Abstract

Osteoradionecrosis (ORN) is a complication seen intermittently in patients who have had radiotherapy to the head and neck, and results of treatment with pentoxifylline and tocopherol (PVe) have been encouraging. As a consequence, some argue that this should be used prophylactically to lower the risk of ORN after dental extractions in this group. We retrospectively analysed data on 390 dental extractions in 82 patients who had had radiotherapy for cancer of the head and neck. Each had been given PVe prophylactically. Only one patient (1.2%) developed ORN (rate/tooth 0.26%). Patients had taken PVe for a mean (SD) of 11 (23) weeks preoperatively and 13.6 (18) weeks postoperatively. The incidence we found was lower than that normally associated with dental extractions in irradiated patients (7%).

Keywords: Osteoradionecrosis; Pentoxifylline; Tocopherol; Dental extractions

Introduction

Osteoradionecrosis (ORN) of the jaws is an uncommon but devastating complication of radiotherapy. Although the diagnosis is self-evident clinically, the diagnostic criteria have not been agreed, the debate being centred around the duration of bony exposure required before diagnosis is accepted. The reported incidence varies between 2% and 22%,[1–3] and a recent systematic review has suggested it to be 7%.[4]

There is also a lack of consensus on the precise pathogenesis of the condition. The hypoxic-hypocellular-hypovascular model, widely accepted as the primary cause,[5] has now been challenged by the theory of radiation-induced fibrosis (RIF) by Delanian and Lefaix,[6] and has led to a new treatment based on antioxidation in the form of pentoxifylline and vitamin E (PVe). Early results have been encouraging.[7–9]

It can be difficult to avoid the onset of ORN in patients who have had radiotherapy for cancer of the head and neck, as the risk increases throughout life. Obvious triggers include dental extractions, but more subtle events, including denture trauma, dental infection, and the insertion of dental implants, have also been implicated. After treatment for oral cancer, the mouth is changed forever, and a dry mouth and a high-

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http://dx.doi.org/10.1016/j.bjoms.2016.02.024

calorific liquid diet both predispose teeth to decay even with the use of high fluoride toothpaste. Apart from good oral hygiene there is no consensus on how to reduce the risk of ORN.

We proposed that PVe may act as a prophylactic agent to reduce the risk of necrosis after dental extractions.[10] The department of oral surgery and head and neck surgery at Guy's Hospital has used PVe since 2008, initially to treat established cases of ORN, but after positive results, as prophylaxis. We report the outcomes of patients who had dental extractions after prophylactic medication with PVe.

Methods

Between 2009 and 2014, 82 patients, who had previously had radiotherapy for cancer of the head and neck, had 390 teeth extracted after careful dental and radiographic examination at the oral surgery department. Patients gave their consent and were started on the standard regimen of pentoxifylline 400 mg twice daily and tocopherol (vitamin E) 1000 IU daily, ideally one month before extraction, and postoperatively, until the socket had healed.

They were all treated under local anaesthesia with or without intravenous sedation or general anaesthesia. We used 2% lidocaine with 1:80000 adrenaline for inferior alveolar nerve blocks, and 4% articaine with 1:200000 adrenaline for infiltrations. Where possible, teeth were extracted in the most minimally traumatic way using luxators, elevators, and forceps, and we raised mucosal flaps to expose the surgical site only as a last resort. A total of 66 patients had extractions without a flap; the remaining 16 required mucoperiosteal flaps. In 55 patients the surgical sites were closed primarily (67%) but only when a series of adjacent teeth were extracted or a mucoperiosteal flap was raised to provide adequate soft tissue for advancement and tension-free closure. When there was insufficient soft tissue for closure (n = 27), the sockets were left to heal by secondary intention. All but 5 patients had antibiotics postoperatively, and chlorhexidine mouthwash was prescribed to 47 postoperatively. All patients were initially reviewed at 2 weeks and subsequent review appointments were made if necessary.

For the purpose of the analysis, the patients were categorised as having a high, moderate, or low risk of ORN after dental extraction. Radiation doses were not used to categorise risk as a large proportion of patients had been treated elsewhere and the information was not available. Extractions on the same side as the primary tumour and in a direct line of the radiation beam, for example, the lower right first molar in a patient with a squamous cell carcinoma (SCC) of the right tonsil, were considered high risk. Those on the contralateral side to the primary tumour in an area in line with the radiation beam - for example, the lower left first molar in a patient with SCC of the right tonsil, were considered to have a moderate risk. Those in an area distant from the site of the primary tumour but still within the radiation field - for example, a posterior mandibular extraction in a patient with SCC of the larynx, were considered to have a low risk. In patients who required multiple extractions, we used the classification of the tooth with the highest risk.

Results

A total of 82 patients (58 men, 24 women), mean age 55 (range 17–83) had 390 extractions (mandible: n = 232, maxilla: n = 158) at a mean of 95 months (range 2-480) after radiotherapy.

Most of the primary tumours were in the oropharynx (25/82, 31%) or the oral cavity (20/82, 24%), but some were in the hypopharynx (n = 14, 17%), nasopharynx (n = 10, 12%), and at other sites (n = 13, 16%). All patients had had radiotherapy to the head and neck: 76 (93%) had had external beam therapy (EBT), and the remaining 6 (7%) intensity modulated radiotherapy (IMRT). Thirty-one (39%) had also had chemotherapy.

The most common reason for extraction was unrestorable radiation caries (57%) followed by apical infection (24%) (Table 1).

Six patients were unable to tolerate the combination of pentoxifylline and tocopherol so 2 had pentoxifylline alone, and 4 tocopherol alone. The remaining 76 followed the standard regimen. Antibiotics were given preoperatively in 30 patients (27%) and postoperatively in 77 patients (94%) (49 patients, 64% had a single antibiotic such as penicillin while the remaining patients had dual antibiotics such as penicillin and metronidazole). The mean (SD) duration of PVe was 11 (23) weeks before and 13.6 (18) weeks after operation.

Table 2 shows details of the groups with a high, moderate, and low risk of ORN. A similar proportion of patients in the high and low risk groups had had chemotherapy. The

Table 1
Underlying dental diagnoses that led to extraction.

Dental diagnosis	No. of patients (n = 82)
Apical periodontitis	20
Unrestorable caries	4
Periodontal disease	10
Irreversible pulpitis	1
Radiation caries	47

Table 2
Breakdown of patients by risk of osteoradionecrosis (ORN). The number in the bracket shows the exact number of teeth extracted in the high-risk region. When patients had multiple extractions, all teeth were classified according to those at highest risk.

Risk of ORN	No. of patients (n = 82)	No. who had chemotherapy (n = 31)	Total extractions (n = 390)
High	30	12	197 (63)
Moderate	18	5	101
Low	34	14	92