SCIENTIFIC ARTICLE

Australian Dental Journal 1999;44:(4):243-247

Hyperbaric oxygen in the prevention of osteoradionecrosis of the jaws

S. Vudiniabola*
C. Pirone†
J. Williamson‡
A. N. Goss§

Abstract

Patients who have had their jaws irradiated as part of management of head and neck malignancy are at risk of osteoradionecrosis (ORN) following tooth extraction. Thirty-seven patients with a history of irradiation to the jaws were managed during a four year period. Twenty-nine patients received hyperbaric oxygen therapy (HBO) consisting of 20 treatments before surgery and ten treatments after. Only one (4 per cent) developed ORN. Seven patients who did not have HBO and one who did (15 per cent) developed ORN. The need for prophylactic treatment with HBO is discussed. It is recommended that prophylactic HBO is used prior to surgery for irradiated facial bones.

Key words: Osteoradionecrosis, hyperbaric oxygen, surgery.

(Received for publication July 1998. Accepted September 1998.)

Introduction

Osteoradionecrosis (ORN) of the facial bones, particularly of the mandible, is a known serious complication of therapeutic radiotherapy for head and neck cancer. ORN is painful, debilitating and frequently refractory to treatment.[1,2] Patients commonly feel it is a worse challenge to their well-being than their original malignancy which required the radiotherapy.

ORN has a varied clinical and radiographic presentation and there is no single diagnostic sign or test. It can be defined as 'an exposure of non-viable irradiated bone, which fails to heal without intervention'.[3] The usual first presentation is pain with subsequent exposure of bone into the mouth. This may progress to wide exposure of bone both into the mouth and through the skin. More advanced stages are associated with constant pain, sequestration, pathologic fracture, malodour, deformity and discharge.[4]

Radiology is not usually helpful in the early stages of ORN[5] and even in its advanced stages does not necessarily relate to the imaging features.[6] Described radiographic features range from normal appearance, to localized areas of osteolysis to extensive osteolysis, sequestra and fracture. Extraction sockets will often remain visible for more than twelve months after surgery.

Computerized tomography (CT) is more valuable in determining the boundaries between normal and non-viable bone.[5] Nuclear medicine scans, usually with technetium 99, will delineate between vascularized and inflamed areas versus non-viable segments.[7] Magnetic resonance imaging has a limited role.

Concepts of the pathogenesis of ORN have undergone change over the last decade. For much of this century ORN was considered primarily an infection,that is,the irradiated bone was injured and became infected.[8] Common traumatic events which breached the overlying mucosa and thus allowed ingress of bacteria were biopsies, cancer surgery, tooth extraction and denture irritation.

Hence treatment of ORN followed the classical principles of infection management; removal of the cause, debridement, drainage and antibiotics.

This concept was challenged by Marx in the early 1980s. He presented the view that ORN was primarily a non-healing wound secondary to endarteritis.[1] The effect of irradiation on the bone

*Formerly Senior Registrar Oral and Maxillofacial Surgery Unit,The University of Adelaide. Currently Consultant Oral and Maxillofacial Surgeon,Suva Hospital, Fiji.
†Clinical Nurse Consultant Hyperbaric Unit, Royal Adelaide Hospital.
‡Associate Professor and Director Hyperbaric Unit, Royal Adelaide Hospital.
§Professor and Director Oral and Maxillofacial Surgery Unit,The University of Adelaide.

Fig 1 . – Patients receiving treatment in the walk-in multiplace chamber.

was to decrease the vascularity and cellularity of both the hard and soft tissues. The tissues became hypoxic and when challenged by a traumatic insult were unable metabolically and nutritionally to respond to the injury. In the hypoxic, injured tissues, macrophages are not stimulated to re-organize the wound, fibroblasts fail to lay down new collagen and a chronic non-healing wound results.[1,3]

Micro-organisms are essentially surface contaminants, and an effect rather than the cause. Thus treatment should be aimed at reversing the hypoxia and increasing the vascularity and cellularity of the tissues.

Hyperbaric oxygen therapy (HBO) is the intermittent, usually daily, inhalation of 100 per cent oxygen at a pressure greater than one atmosphere absolute (ATA).[9] It is a means of increasing the dose of oxygen dissolved in the plasma and tissues which reduces hypoxia within the affected tissues and stimulates angiogenesis in the hypovascular tissue. HBO is delivered by sessions within a hyperbaric chamber, which may range from a small monoplace chamber for one patient to a multiplace chamber which holds several patients and an attendant (Fig. 1). A single HBO session for ORN treatment commonly consists of the patient breathing 100 per cent pure oxygen at 2-2.4 atmospheres for 90-120 minutes. Usually treatments occur on a daily basis, five to six days per week, until the required number of sessions is completed.

The mechanism of action of HBO on non-healing wounds is complex. Regular, periodic, but not sustained, elevation of the oxygen within hypoxic tissues has been shown to enhance the killing ability of leucocytes,[10] to stimulate fibroblast growth, increase collagen formation and to promote growth of capillaries.[11] It is also toxic to aerobic and anaerobic bacteria, and inhibits bacterial toxin formation.[12] Aminoglycoside antibiotics are also enhanced in their antibacterial activity.

The reported incidence of ORN of the mandible varies widely, ranging from 2-39 per cent.[3,13] This variation depends in part on the techniques of radiotherapy used,in particular the radiation dose to the bone, but also on the veracity of the audit. Generally, the incidence of ORN has reduced over the last three decades. This relates to improvements in radiation technique and to the standard of pre-irradiation dental care and ongoing management.[2]

Table 1. Patient characteristics

	HBO group n=29	Control group n=7
Age (mean and range)	52.6 (20-73)	56.3 (47-64)
Under 50	8	1
Over 50	21	6
Sex		
Male	20	6
Female	9	1
Malignancy type		
SCC	19	6
Other	10	1
Malignancy site		
Oral	15	4
Pharyngeal/laryngeal	8	1
Salivary gland	4	1
Other	2	1
Previous surgical treatment		
No surgery	6	0
Local	8	1
Radical	15	6
Previous radiotherapy		
<55 Gy	10	0
>55 Gy	14	3
Not known	5	4

Table 2. Reason for inclusion in the control group

Residual lung disease	1
Previous HBO within six months	1
Declined consent	1
Claustrophobia in the chamber	3
Barotrauma after two dives	1

Table 3. Treatment received by both groups

	HBO group n=29	Control group n=7
HBO treatment		
Less than 30 dives (pre-surgery 8-23) (post-surgery 0-3)	5	0
30 dives	21	0
More than 30 dives (38-50)	3	0
Surgery		
Extractions	22	5
Resection	2	1
Plate removal	1	1
Implant placement	4	0

Table 4. Outcome of treatment for both groups

	HBO group n=29	Control group n=7
Fully healed	28 (96%)	6 (85%)
ORN developed	1 (4%)	1 (15%)

The relationship between dental disease in dentate patients who have head and neck radiotherapy and subsequently develop ORN has been shown in a number of studies.[14,15] When dental care programmes to improve dental health prior to irradiation and then to maintain it subsequently are introduced, the incidence of ORN falls. Edentulous patients have a lower rate of ORN and often have a more limited involvement.

Tooth extraction is the most common cause of trauma-induced ORN in the jaws. It has been reported as the trigger for mandibular ORN in 60-89 per cent of cases.[3,14,15] In the authors' series of 12 consecutive cases of mandibular ORN, nine (75 per cent) followed tooth extraction.‖

Hence, when confronted with a patient who has had full dose or more than 55 Gy radiotherapy to the jaws and who requires tooth extraction, then prophylactic treatment with HBO has been proposed.[16] Thus the hypoxia is decreased prior to the tissue insult by 20 HBO treatments with a further 10 sessions post-surgery. This regimen has been evaluated in a trial where patients with irradiated jaws requiring extractions were randomized to a prophylactic HBO group and a control group which received antibiotics only. The HBO group had an ORN incidence of 5.4 per cent and the antibiotic group 29.9 per cent.[16] No other similar studies attempting to replicate this result were found in the literature.

The aim of this study was to evaluate the effect of HBO as a prophylactic treatment for patients with irradiated jaws requiring oral surgery.

‖Vudiniabola S, Pirone C, Williams J, Goss AN. Hyperbaric oxygen in the treatment of osteoradionecrosis of the facial bones. (In preparation.)

Table 5. Hyperbaric experience

	Better %	Same %	Worse %
Overall	58	37	5
Eating ability	11	74	5
Talking	11	84	5
Jaw opening	21	74	5
Mouth dryness	32	53	16
Pain	37	58	5

Materials and methods

All patients presenting to the Oral and Maxillofacial Surgery Unit at The University of Adelaide over a four year period (1992-96) who had a previous history of head and neck irradiation to the jaw region and who required oral surgical procedures were included in this prospective trial. This trial was conducted in accordance with the requirements of the Research Ethics Committees of the Royal Adelaide Hospital and The University of Adelaide.

The previous irradiation history was determined and it was confirmed that they had received 50-66 Gy to the region of the jaws. A full dental examination was performed and those teeth requiring extraction were determined. The remaining dentition was made dentally fit by restorations and periodontal treatment.

The fitness for HBO therapy was determined. The treatment proposal was described to the patient and informed consent obtained.

The HBO treatment required was 20 sessions each at 2.4 ATA for 90 minutes, followed by a 30 minute ascent back to one ATA. This is known technically as a 14/90/30 cycle. This was followed by surgery and then 10 further 14/90/30 sessions. Patients who did not receive this HBO therapy for any reason were included and acted as the control group.

Follow-up examinations were performed at six-monthly intervals. Oral status and function, radiographic appearance, and any signs of ORN or oral cancer recurrence were determined.

The patient's opinion of the experience was determined. Data collected were coded and computerized for descriptive statistics. Variables were assessed by mean value, standard error and standard deviation. The Student's *t* test was used to determine differences between groups.

Results

Thirty-seven patients met the inclusion criteria for this study. Seven patients did not have an effective course of HBO prior to surgery, either because they did not consent, or had contraindications, or developed HBO complications early in the course of treatment. This group constituted the control group. Twenty-nine patients had a full course of HBO and

Table 6. Pre-radiotherapy dental protocol

1. Radiotherapy consultation for head and neck cancer
   - All patients automatically referred for dental consultation
2. Dental consultation
   - Examination and radiographs
   - Aim is to determine whether it is possible to conserve teeth for the rest of the patient's life
   - Extractions are indicated for:
     - widespread caries
     - unrestorable teeth
     - patients who have no intention or capability of following a lifetime conservation plan
   - If doubt exists, then extract
3. Radiotherapy – dental discussion
   - The nature of the radiotherapy and dental treatment priorities need to be discussed
4. Dental treatment
   - All surgery prior to radiotherapy
   - Primary closure of all wounds
   - Treatment must be urgently instituted; cancel non-cancer patients rather than delay
5. Radiotherapy treatment
   - Once instituted,do not intermit for dental treatment
   - Oral advice and care for stomatitis
6. Dental review and treatment
   - Maintenance programme for life
   - If subsequent extractions then follow post-radiotherapy protocol

Table 7. Post-radiotherapy protocol

1. Dental presentation
   - History and examination confirms history of head and neck radiotherapy and oral problems
2. Urgent referral to the Head and Neck Dental Co-ordinator
   - Liaise with radiation oncology to confirm radiation dose and field
   - Review patient to confirm treatment need
3. At risk of ORN if:
   - Need extractions
   - Had 50 Gy + to jaws
4. OMFS and hyperbaric consultation
   - 20 HBO treatments
   - Surgery
   - 10 HBO dives
5. Dental review and treatment
   - Maintenance programme for life

surgery. This group was the experimental group. One patient commenced HBO, had early complications and refused to have any more treatment so was excluded from the study.

The patient characteristics of the control and experimental groups are shown in Table 1. The reasons for patients in the control group not proceeding with HBO therapy are shown in Table 2. The types of treatment received by the control and experimental groups are shown in Table 3. The outcome of treatment to both groups is shown in Table 4.

The patient's opinion of the experience of having HBO as well as surgery is shown in Table 5. Generally, 14 respondents (68 per cent) felt HBO treatment was a bearable experience, 5 (26 per cent) found it pleasurable and one patient (5 per cent) felt it was unbearable. This patient exhibited pulmonary oxygen toxicity.

Discussion

This study showed that prophylactic HBO treatment reduced the risk of ORN developing following surgery to irradiated jaws. This is a worthwhile benefit as ORN is painful, debilitating and difficult to treat.[1,2]

There are aspects of this study which can be criticized. Firstly, the numbers are small. This, however, reflects both the patient pool and the treatment protocols which have been in place for head and neck radiotherapy patients in Adelaide. All have rigorous pre-irradiation dental examination and treatment so that they are dentally fit (Table 6, 7). Thus, the number of extractions required after radiotherapy is low. Scientifically, it would have been better to randomize HBO and non-HBO into two equal groups. This, however, would not have been ethical as the world literature does show that HBO is beneficial. Hence the control group was not randomized but consisted of those unsuitable to receive a full HBO course.

Adding HBO to the treatment regimen does add time, expense and risk to dental treatment. The time involves daily attendance six times a week for 20 HBO sessions prior to surgery. Within a few days of recovery a further 10 daily visits for further HBO sessions are required. Although each session takes approximately 120 minutes, practically, this takes up to half of the day in travelling and waiting. The cost of providing a session for up to six patients in a busy hyperbaric unit in a public hospital, when amortized over the capital cost of equipment, staff, etc., is currently $422. Thus the impact of this treatment on the overall health budget is $12 500.¶ Although HBO is a benign treatment, there is a morbidity.[17] The most common are barotrauma to the ear and, less commonly, sinus pain. Some patients have changes in ocular refraction but this usually spontaneously resolves. The most common mild problem in this study was claustrophobia but changing to a larger multiplace chamber resolved this in the latter part of the study (Fig. 1). Most patients in the study found that the HBO experience was bearable and, for a quarter, pleasurable. Not surprisingly, the only patient who found it unbearable had pulmonary oxygen toxicity.

The disadvantages of HBO treatment need, however, to be weighed against the known risks of not using HBO. Dental extraction is the most common trigger of ORN of the jaws.[8] Treatment of established ORN is a long, slow and ineffective process. Success

¶Williamson J. Internal audit of the costs of the RAH Hyperbaric Unit. (Unpublished.)

rates of less than 50 per cent are common. The cost of such treatment was estimated as being in excess of $50 000.[18] Treatment of ORN with HBO is considerably more successful but requires extensive treatment, both surgically and in the number of HBO sessions.

The lessons of this study to the practising dentist are clear. One must know if patients have had radiotherapy to the jaws. If so, one does need to know the dose and the field. Dosage of 55 Gy or greater to the jaws does put the patient at risk of ORN.[15] The less recent the radiotherapy, the greater the risk, as radiotherapy damage does not wear off.

Dental treatment for patients who have had radiotherapy to the jaws should be aimed at conserving teeth. However, if the patient was not dentally fit prior to radiotherapy, has widespread smooth surface caries secondary to radiation xerostomia or has no intention or ability to follow a conservation dental programme, then extraction is indicated. If extractions are indicated, then one is better to clear all unsaveable teeth rather than one at a time.

Prior to commencing dental treatment, it is appropriate to seek advice. Most head and neck clinics have oral and maxillofacial surgeons and general dentists as part of the team. They can provide advice on the availability of hyperbaric oxygen facilities. Currently, for sound medical and economic reasons, such facilities are confined to the major metropolitan centres where most of the major head and neck cancer clinics are situated.

Rural patients may be resistant to returning to the major treatment centre unless they have a fully informed understanding as to why the apparently simple treatment of tooth extraction needs to be approached with care. Some radiotherapists will still advocate prophylactic antibiotics as being sufficient but there is no evidence of any prophylactic benefit from antibiotics. Further, it shows a lack of understanding of the pathogenesis of ORN.

Thus, the optimum management for those who require extractions or other surgery to irradiated jaws should include prophylactic HBO. Clearly, prevention is better than cure.

References

1. Marx RE. Osteoradionecrosis. A new concept in its pathophysiology. J Oral Maxillofac Surg 1983;41:283-288.
2. Epstein JB, Wong FL, Stevenson-More P. Osteoradionecrosis: Clinical experience and a proposal for classification. J Oral Maxillofac Surg 1987;45:104-110.
3. Marx RE, Johnson SP. Studies in the radiobiology of ORN and their clinical significance. Oral Surg Oral Med Oral Pathol 1987;64:379-390.
4. Fleming TJ. Oral tissue changes of radiation oncology and their management. Dent Clin North Am 1990;34:223-237.
5. Miles DA. Imaging inflammatory disorders of the jaw: Simple osteitis to generalised osteomyelitis. Oral Maxillofac Surg Clin North Am 1992;1:207-221.
6. Guttenberg SA. Osteoradionecrosis of the jaws. Am J Surg 1974;127:326-330.
7. Hutchinson IL, Cullum ID, Langford JA, Jarrit PH, Harris M. The investigation of ORN of the mandible by 99m TC methylene diphosphonate radionucleotide bone scans. Br J Oral Maxillofac Surg 1990;28:143-149.
8. Meyer I. Infectious diseases of the jaw. J Oral Surg 1970:28:17-26.
9. Cianci P, Sato R. Adjunctive hyperbaric oxygen therapy in the treatment of thermal burns:A review. Burns 1994;20:5-14.
10. Hunt TK, Pai MP. Effect of varying ambient oxygen tensions on wound metabolism and collagen synthesis. Surg Gynecol Obstet 1972;135:561-568.
11. Knighton DR,Silver IA,Hunt TK.Regulation of wound healing, angiogenesis-effect of oxygen gradient and inspired oxygen concentrations. Surg 1981;90:262-269.
12. Mader TJ, Brown GL, Guckian JC, Wells CH, Reinarz JA. A mechanism for the amelioration of hyperbaric oxygen of experimental staphylococcal osteomyelitis in rabbits. J Infect Dis 1980;142:915-920.
13. Daly TE, Drane JB. Proceedings: The management of teeth related to the treatment of oral cancer. Proc Natl Cancer Conf 1972;7:147-154.
14. Beumer J III, Silverman S Jr, Berak SB Jr. Hard and soft tissue necrosis following radiation therapy for oral cancer. J Prosthet Dent 1972;27:640-647.
15. Murray CG, Daly TE, Zimmerman SO. The relationship between dental disease and radiation necrosis of the mandible. Oral Surg Oral Med Oral Pathol 1980;49:99-104.
16. Marx RE, Johnson RP, Kline SN. Prevention of osteoradionecrosis: A randomized prospective clinical trial of hyperbaric oxygen versus penicillin. J Am Dent Assoc 1985;111:49-54.
17. Kindwall EP. Hyperbaric medicine practice. Arizona: Best Publishing, 1995:1-254.
18. Vudiniabola S. Hyperbaric oxygen therapy in the treatment and prevention of osteoradionecrosis. Adelaide: The University of Adelaide, 1997:172.MDS thesis.

Address for correspondence/reprints:
Professor Alastair N. Goss,
Oral and Maxillofacial Surgery Unit,
The University of Adelaide, South Australia 5005.