Indian J Otolaryngol Head Neck Surg
DOI 10.1007/s12070-013-0640-z

ORIGINAL ARTICLE

A Retrospective Study of Outcomes in Subjects of Head and Neck Cancer Treated with Hyperbaric Oxygen Therapy for Radiation Induced Osteoradionecrosis of Mandible at a Tertiary Care Centre: An Indian Experience

Puneet Gupta · Tarun Sahni · G. K. Jadhav · Sapna Manocha · Shweta Aggarwal · Sapna Verma

Received: 3 January 2013 / Accepted: 6 March 2013

Abstract Osteoradionecrosis (ORN) of the mandible is a rare complication of radiation therapy for head and neck cancer. It manifests as an area of exposed necrotic bone failing to heal for at least 3 months. Our study aims to determine the effectiveness of HBO in management of radiation induced mandibular ORN. A retrospective study of 33 subjects of mandibular ORN treated with HBOT during period 2009–2011 was carried out. The mean patient age was 60 years (range 41–80).They were treated in a multiplace hyperbaric chamber at 2.4 ATA, for 90 min once a day for up to 30 sessions. Pre and post treatment improvement in relation to symptoms, healing of intraoral wound and overall wellbeing were evaluated. Out of 33 Subjects, 48 % ($n = 16$) cases showed complete healing of wound, 18 % ($n = 6$) had marked healing, slight healing in 24 % ($n = 8$) cases and 9 % ($n = 3$) cases had no change in healing. 70 % (23 of 33) cases had significant reduction in pain, 62 % (18 of 29) cases had improved jaw opening, 41 % (11 of 27) cases and 71 % (20 of 28) cases showed improvement in ability to talk and mouth dryness respectively. Overall 85 % (28 of 30) cases showed improvement. Our clinical experience supports the efficacy of HBO treatment for radiation induced mandibular ORN and we recommend additional multicentric, prospective studies to be carried out defining the role of HBOT using at least 30 sessions in such cases.

Keywords Osteoradionecrosis · Hyperbaric oxygen · Mandible · Wound · Neck cancer

P. Gupta
Department of Oncology, Indraprastha Apollo Hospital, Sarita Vihar, Delhi-Mathura Road, New Delhi 110076, India

T. Sahni (✉)
Department of Internal and Hyperbaric Medicine, Indraprastha Apollo Hospital, Sarita Vihar, Delhi-Mathura Road, New Delhi 110076, India
e-mail: aimhu@live.in

G. K. Jadhav · S. Manocha
Department of Radiation Oncology, Indraprastha Apollo Hospital, Sarita Vihar, Delhi-Mathura Road, New Delhi 110076, India

S. Aggarwal · S. Verma
Department of Hyperbaric Medicine, Indraprastha Apollo Hospital, Sarita Vihar, Delhi-Mathura Road, New Delhi 110076, India

Introduction

Mandibular Osteoradionecrosis (ORN) is a serious, debilitating and/or deforming complication of radiation therapy after the treatment of head and neck cancer. When ORN develops, bone within the radiation field becomes devitalized and may be exposed through the overlying skin or mucosa, persisting as a non healing wound for 3 months or more [1, 2].

According to Marx's concept [3], pathogenesis of ORN is a result of hypovascular, hypocellular and hypoxic tissue formation leading to a non healing wound with mandible as the most common site being affected. Depending on multiple risk factors such as age, primary tumor site, treatment type (e.g.; external beam radiotherapy, brachytherapy, surgery, chemotherapy or combinations), and radiation dose, mandibular ORN occurs in 10–15 % of head and neck cancer irradiated patients [3–6].

The treatment of ORN aims to eliminate the pain, control infection and reduce its spread. Its conservative management consists of antibiotics, antiseptics and small sequestrum removal. In recent years, healing of ORN has

Published online: 31 March 2013

focused on revascularization of irradiated tissues and improving compromised microcirculatory condition [5–9]. Based on these newer concepts of pathophysiology of ORN, hyperbaric oxygen therapy (HBOT) is utilized as an adjunctive treatment in its management and has emerged as a potential primary option for such challenging conditions [10–12]. HBOT assists in the repair of radiation induced damage by improving oxygenation of tissue, promotes neovascularization and help eradicate bacteria in damaged tissue of radiation treated patients [12–15].

Materials and Methods

The medical records of 42 adult patients with head and neck cancer having radiation induced mandibular ORN treated at the hyperbaric oxygen Therapy Unit, Indraprastha Apollo Hospital, New Delhi (India) were reviewed retrospectively. The HBO unit at this tertiary care hospital has been treating patients referred with ORN since 2000. However, this study analyses the data of patients treated between 2009–2011.

After excluding 9 patients for incomplete records or inadequate treatment course of up to 10 HBOT sessions, 33 patients were included in the study. All patients had history of irradiation for head or neck cancer and were referred to HBO unit for likely induced mandibular osteoradionecrosis. The patients with Marx Stage I alone were included in the study.

The diagnosis of ORN was based on patient's history, clinical and radiographic findings. The criteria assessed included age of patient, gender, malignancy site, time between radiotherapy, onset of ORN and follow up period. The minimum patient follow up time for inclusion in the study was 12 months and incidence of recurrence of malignancy in any of these patients was recorded. These patients received HBOT along with wound care and appropriate supportive treatment as prescribed by their referring oral surgeon or oncologist.

HBOT was delivered once daily in a multiplace chamber at a pressure of 2.4 atmosphere absolute (ATA) for 90 min, 6 days a week for up to 30 consecutive sessions. The treatment was deemed successful if following criteria were met: (a) healing of intraoral wound (b) improvement in symptoms and (c) improvement in overall well being. The change in overall well being was classified as 3 groups: (i) Good, improvement in ≥ 3 symptoms (ii) Fair, improvement in 2 symptoms (iii) Poor, improvement in <2 symptoms or even deterioration during the treatment.

Results

Thirty-three patients met the inclusion criteria for this study. The patients included in our study presented to our unit within 1 year of onset of mandibular ORN symptoms including one or the other i.e.; presence of intraoral wound, pain, reduced eating ability, mouth dryness, ability to talk and restricted jaw opening Table 1.

There were 26 males and 7 females with mean age of 59.8 years (range from 41–80 years). The estimated radiation dosage ranged from 5,000–7,000 gray given either alone or in combination with chemotherapy or surgery in once daily fractionation of 180–200 cGy. These patients had primary tumors of tongue ($n = 13$), floor of mouth ($n = 3$), palate ($n = 2$), larynx ($n = 7$), pharynx ($n = 3$) and alveolus ($n = 5$).

ORN of mandible developed between 3 months to 1 year (mean time of 7.5 months) after completion of radiation therapy. With regard to patient's performance status, none of the patients were medically compromised and had Karnofsky status of up to 2. Patients were followed up to 12 months after completion of HBO therapy. The improvement in healing of intraoral wound after 30 sessions of HBOT (Table 2). The complete wound healing occurred in 48 % ($n = 16$) cases, marked improvement was seen in 18 % ($n = 6$) cases, 24 % ($n = 8$) cases had slight improvement and 9 % ($n = 3$) patients did not show any change as they withdrew from the study before HBO treatment completion.

Regarding the improvement in symptoms after treatment, 70 % (23 of 33) cases had significant reduction in

Table 1 Clinical characteristics of the patients with ORN included in the study

Variable	$n = 33$	%
Sex		
Male	26	79
Female	7	21
Age group (years)		
≤ 50	5	15
>50	28	85
Mean age	59.8 years	
Median	59	
Incidence of ORN according to malignancy site		
Tongue	13	39
Floor of mouth	3	9
Palate	2	6
Larynx	7	21
Pharynx	3	9
Alveolus	5	15
Prior anticancer treatment in patients with ORN		
Radiotherapy alone	6	18
Radiotherapy + chemotherapy	7	21
Post op radiotherapy	16	48
Pre & post op radiotherapy	4	12

Table 2 Improvement in healing of intraoral wound in patients after HBO treatment

Improvement in healing	$n = 33$	%
Complete healing	16	48
Marked improvement	6	18
Slight improvement	8	24
No change	3	9

Table 3 Improvement in symptoms after treatment in patients with ORN

Symptom	*n*	%
Pain (difference of >3 on VAS)	23/33	70
Reduced eating ability	14/27	52
Mouth dryness	20/28	71
Ability to talk	11/27	41
Restricted jaw opening	18/29	62

Table 4 Overall improvement in patients after HBO treatment

Overall improvement	$n = 33$	%
Good	11	33
Fair	17	52
Poor	5	15

Good improvement in ≥3 symptoms, *Fair* improvement in 2 symptoms, *Poor* improvement in <2 symptoms

pain, 52 % (14 of 27) cases had improvement in eating ability, dryness of mouth was reduced in 71 % (20 of 28) cases, 41 % (11 of 27) and 62 % (18 of 29) cases showed improvement in ability to talk and opening of jaw respectively (Table 3).

The change in overall well being, 'Good' recovery after hyperbaric oxygen therapy was observed in 33 % ($n = 11$) cases, 'fair' recovery in 52 % ($n = 17$) cases and poor recovery was seen in 15 % ($n = 5$) cases (Table 4). The reason attributed to poor recovery might be due to withdrawal of 3 patients from the treatment, irregular sessions of HBOT in 1 patient and one patient had recurrence of tumor.

The statistical analysis in our study was based on the intent to treat principle.

Discussion

Management of irradiated patients with cancer in the head and neck region represents a challenge for multi-disciplinary teams [1–5]. Mandibular ORN is the most severe sequelae caused by radiotherapy [6–9]. The management of this side effect is difficult and can result in bone or soft tissue loss, affecting the quality of life. ORN is characterized by delayed bone repair secondary to damage caused by radiotherapy developing over a period ranging from 4 months to several years after radiotherapy [10–13]. The clinical management of ORN normally comprises medical care, avoidance of tobacco use in any form, improvement of dental hygiene, the control of infections and removal of the necrotic tissue with more aggressive surgery.

ORN becomes clinically significant when it develops at four anatomic sites: chest wall, mandible, pelvis, vertebral column, and skull [14]. Because of the mandible's low vascularity and great density, the incidence of ORN is highest at this site. The mandible is often involved because head and neck cancers patients in India usually have radiation therapy in the multimodal treatment approach [15–17].

Our study included patients with Marx I stage criteria i.e.; who met the definition of ORN except those with cutaneous fistulae, pathologic fracture, or radiographic evidence of bone resorption because Marx II and III stage Patients are essentially treated by conventional surgery.

The keystone of the treatment for ORN is the provision of adequate tissue oxygenation in the damaged bone [18, 20]. HBOT is the modality to accomplish this and is considered as a primary part of all therapies for ORN. The rationale for the use of HBO in irradiated tissue is to increase the blood to tissue oxygen tension enhancing the diffusion of oxygen into the tissues [19, 20]. This revascularizes the irradiated tissue and improves the fibroblastic cellular density.

In recent years, healing of ORN has been focused on revascularization which involves providing adequate nutrition and oxygen to radiation devascularized tissue [24]. McKenzie et al. [19] published treatment with HBO of post radiation ORN of the mandible in 26 patients and concluded that resolution occurred in 69 % (18 of 26) patients. In our study complete healing of intraoral wound was achieved in 16 out of the 33 Patients.

The benefits of revascularization of irradiated tissues have been shown in many clinical and experimental studies. In 1973 Greenwood & Gilchrist [11] reported for the first time the benefits of HBO on wound healing in post radiation patients. Our study demonstrates improvement in symptoms with up to 30 sessions of HBOT. 70 % cases had significant reduction in pain, 52 % cases had improvement in eating ability, dryness of mouth was reduced in 71 % patients, 41 % cases and 62 % cases showed improvement in ability to talk and opening of jaw respectively.

This resulted in overall change in these patients with favorable recovery in majority 85 % cases. Good recovery was seen in 33 % cases with only 15 % patients showing poor recovery.

Our study does not exclude the adjunctive use of antibiotics, local wound care and nutritional support however our treatment results suggests HBOT should be one of the primary treatment modalities for mandibular ORN to improve the quality of life in these patients.

We recommend multicentric, prospective trials be carried out to establish role of HBOT in mandibular ORN patients and to identify specific groups of patients likely to benefit from the addition of this therapy.

Conflict of interest No conflict of interests exist.

References

1. Peterson DE, Doerr W, Hovan A, Pinto A, Saunders D, Elting LS et al (2010) Osteoradionecrosis in cancer patients: the evidence base for treat-ment-dependent frequency, current management strategies, and future studies. Support Care Cancer 18:1089–1098
2. Pitak-Arnnop P, Sader R, Dhanuthai K, Masaratana P, Bertolus C, Chaine A et al (2008) Management of osteoradionecrosis of the jaws: an analysis of evidence. Eur J Surg Oncol 34:1123–1134
3. Marx RE (1984) Osteoradionecrosis of the jaws: review and update. Hyperb Oxyg Rev 5:78–126
4. Bennett MH, Feldmeier J, Hampson N, Smee R, Milross C (2005) Hyper-baric oxygen therapy for late radiation tissue injury. Cochrane Database Syst Rev 3:CD005005
5. Bedwinek JM, Shukowsky LJ, Fletcher GH, Daley TE (1976) Osteoradionecrosis in patients treated with definitive radio-therapy for squamous cell carcinomas of the oral cavity and naso and oropharynx. Radiology 119:665–667
6. Curi MM, Dib LL (1997) Osteoradionecrosis of the jaws: a retrospective study of the background factors and treatment in 104 cases. J Oral Maxillofac Surg 55:540–544
7. Epstein J, Meij E, McKenzie M, Wong F, Lepawsky M, Stevenson-Moore P (1997) Postradiation osteoradionecrosis of the mandible. A long-term follow-up study. Oral Surg 83:657–662
8. Epstein JB, Rea G, Wong FLW, Spinelli J, Stevenson-Moore P (1987) Osteoradionecrosis: study of the relationship of dental extractions in patients receiving radiotherapy. Head Neck Surg 10:48–54
9. Epstein JB, Wong FLW, Stevenson-Moore P (1987) Osteoradionecrosis: clinical experience and a proposal for classification. J Oral Maxillofac Surg 45:104–110
10. Fattore L, Strauss RA (1987) Hyperbaric oxygen in the treatment of osteoradionecrosis: a review of its use and efficacy. Oral Surg 63:280–286
11. Greenwood TW, Gilchrist AG (1973) The effect of HBO on wound healing following ionizing radiation. In: Trapp WC (ed) Proceedings of the fifth international congress on hyperbaric medicine, vol 1. Barnaby, Canada: Simon Frasier University, pp 253–263
12. King GE, Scheetz J, Jacob RF, Martin JW (1989) Electrotherapy and hyperbaric oxy-gen: promising treatments for postradiation complications. J Prosthet Dent 62:331–334
13. Kluth EV, Jain PR, Stuchell RN, Frich JC (1988) A study of factors contributing to the development of osteora-dionecrosis of the jaws. J Prosthet Dent 59:194–201
14. Mainous EG, Hart GB (1975) Osteora-dionecrosis of the mandible treatment with hyperbaric oxygen. Arch Otolaryngol 101:173–178
15. Mainous EG, Hart GB (1976) The treatment of radiation necrosis with hyperbaric oxygen. Cancer 37:2580–2585
16. Mansfield M, Sanders D, Heimbach R, Marx R (1981) Hyperbaric oxygen as an adjunct in the treatment of osteoradionecrosis of the mandible. J Oral Maxillofac Surg 39:585–589
17. Marx RE, Johnson RP (1987) Studies in the radiobiology of osteoradionecrosis and their clinical significance. Oral Surg 64:379–390
18. Marx RE (1983) Osteoradionecrosis: a new concept of its pathophysiology. J Oral Maxillofac Surg 41:283–288
19. Merkesteyn JPR, Bakker DJ, Borgme-ijer-Hoelen AMMJ (1995) Hyperbaric oxygen treatment of osteoradionecrosis of the mandible. Experience in 29 patients. Oral Surg 80:12–16
20. McKenzie M, Wong F, Epstein J, Le-pawsky M (1993) Hyperbaric oxygen and post-radiation osteonecrosis of the mandible. Eur J Cancer 29(B):201–207