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ORIGINAL ARTICLE

Role of Hyperbaric Medicine for Osteoradionecrosis and Post Irradiation Wounds: an Institutional Experience

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Abstract

To study the effectiveness of hyperbaric medicine in osteoradionecrosis and irradiation induced wounds. To evolve a protocol for management with combined surgical modality for irradiation induced injury. This study was carried out in the Plastic Surgery Department, from November 2011 to December 2018. A total of 30 patients with post irradiation patients subjected to hyperbaric oxygen therapy during the management were enrolled in the study. The results regarding the changes in wound and complications were noted. Out of 30 patients, 20 patients were with radiation injury involving the oral cavity, one patient with left lower limb, one with breast, 3 with radiation injury of cheek, 3 of mandible, one with radiation cystitis and one involving the tooth socket. One patient experienced reversible myopia as a complication of hyperbaric therapy. No other complications were noted. Hyperbaric therapy is a useful adjunct for surgery in management of osteoradionecrosis and post irradiation wound and proves therapeutic in some post irradiated wound where we cannot offer surgical correction.

Keywords Hyperbaric medicine · Osteoradionecrosis · Post irradiation wounds

Introduction

Radiation-related complications after malignancy are more common due to the cellular hypoxia, progressive endarteritis of the minor blood vessels and damage to the normal healing process in the irradiated tissue. Discoloration, ulceration and necrosis are common in this irradiated tissue. With this presentation, unfortunately the treatment failure is high, as there is a compromised blood supply and inherent inability of the radiated tissue to heal. Hyperbaric oxygen therapy with the mechanism of oxygen-induced angiogenesis modifies the tissue damages incurred by radiation injury and promotes healing in the irradiated tissue [1].

Craighead et al. [2] conclude that hyperbaric oxygen therapy is likely effective and should be applied in refractory disorders. HBO2 may provide symptom resolution in certain complications of radiation and may reduce complications when combined with surgery removing tissues and organs affected by necrosis.

Materials and Methods

The study was conducted in the Department of Plastic Surgery and burns. Thirty patients with post irradiation following tumour were screened for inclusion in the study from November 2011 to December 2018. Patients requiring ICU/ventilator support were not included in the study. Informed consent was obtained from the patients undergoing the study. Wound care and surgical management was undergone as per the standard protocol of the unit. After initial assessment, patient was treated with hyperbaric oxygen therapy according to the protocol described below.

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HBO Protocol for Radiation Wound

Marx protocol, a multidisciplinary surgical and hyperbaric staged management of mandibular ORN, significantly reduced the incidence of post-operative infection, dehiscence, and healing delays [3, 4].

ORN Prevention Protocol (Marx 20/10 Protocol)

HBO prophylaxis before tooth extraction or dental implants in irradiated jaw is usually referred to as a “20/10 protocol” with 20 sessions of HBO at 2.5 ATA for 90 min on 100% oxygen prior to surgery, followed by 10 such sessions after surgery [3].

ORN Treatment Protocol (Marx 30/10 Protocol)

Marx [5] established a protocol associating surgery and HBO; it consists of three stages. In stage I, after 30 sessions (100% oxygen, 2.4 ATA, 90 min/day, 5 day/week), wound is re-examined: in case of improvement, the patient completes a full course of 60 sessions. If there is no improvement, the patient is advanced to stage II: a sequestrectomy with primary closure is accomplished, with HBO if healing progresses without complication. If the wound dehisces, the patient is advanced to stage III: a resection is accomplished. In a patient whose initial presentation includes pathologic fracture, orocutaneous fistulae, or radiographic evidence of resorption to the inferior border, an initial course of 30 sessions is given and the patient directly enters in stage III. In stage III-R, 10 weeks after resection, the patient is given an additional 20 sessions in preparation for bone graft reconstruction.

Results

Mean age of patients subjected to hyperbaric therapy was 58.9 years. There were 25 males and 5 females (Table 1). Out of 30 patients, 27 patients were with radiation injury involving the oral cavity (cheek, 3; mandible, 3; tooth socket, 1), one patient with left lower limb, one with breast and one with radiation cystitis. One patient experienced reversible myopia as a complication of hyperbaric therapy. No other complications were noted. Mean number of session was 16.7. Hyperbaric oxygen therapy was administered as per the indication of Undersea Hyperbaric Medicine Society. Marx protocol as described previously was applied in cases of dental extraction and surgical cases; in other cases hyperbaric oxygen therapy was given to prevent the tissue damage associated with radiation therapy.

Clinical Applications

Case 1

A 30-year-old female with radiation to the head and neck area following a nasopharyngeal malignancy had documented low tissue oxygen over the area of the mandible on which she requires a molar extraction (Fig. 1a, b). She received 2 weeks of HBOT at 2.4 ATA daily once for 2 weeks at which here tp02 was 30 mm (Fig. 1c). She underwent dental extraction and followed it with further 14 sessions after which her tissue oxygen levels improved to 65 mm (Fig. 1d). The patient was then subjected to dental extraction (Fig. 1e).

Case 2

A 70-year-old gentleman following irradiation developed osteoradionecrosis of the mandible (Fig. 2a). He received 28 sessions of HBO, and after improvement of tissue oxygenation, a local mucosal flap was utilized to cover the defect (Fig. 2b). Donor area was closed primarily (Fig. 2c). Wound healed completely without any complication.

Case 3

A 69-year-old gentleman had necrosis of the nasolabial flap following submucous fibrosis due to radiation injury (Fig. 3a). His injured tissue was subjected to initial wound debridement and hyperbaric oxygen therapy (Fig. 3b) initially and then taken up for closure by local cheek rotation flap at a later date (Fig. 3c–e).

Discussion

Osteoradionecrosis (ORN) is defined as an area of non-healing exposed bone in a patient with a history of radiation therapy that persists for more than 3 months without any evidence of tumour recurrence. Beyond the targeted tumour cells, radiation also destroys the nearby normal cells and blood vessels. Soft tissue and bone exposed to radiotherapy undergo progressive obliterative endarteritis with tissue hypoxia and ischaemia [6]. Aetiology of ORN was considered primarily to be an avascular aseptic necrosis rather than the result of infection. In a patient of head and neck cancer, who has been exposed to radiation strength between 2000 and 5000 rads, there is a high possibility of bone and soft-tissue damage due to radiotherapy with subsequent difficulties in healing. Above the radiation strength of 5000 rads, healing of any subsequent surgical wound will be a definite problem. Since most of the reconstruction of head

Table 1 Patients treated for post radiation injury with hyperbaric oxygen therapy

S.no	Age/ sex	Disease	No. of sessions	Radiation therapy	Complications due hyperbaric oxygen therapy
1	59/M	Post radiation necrosis–oral cavity	12	66Gy in 33# 3DCRT	NIL
2	71/F	Radiation cystitis and proctitis	17	45 Gy 23 # 3DCRT followed by brachytherapy 8 Gy to point A 3 sittings	NIL
3	61/F	Post radiation necrosis–oral cavity	12	66Gy in 33# 3DCRT	NIL
4	27/F	Post radiation necrosis–tooth socket	6	66Gy in 33# 3DCRT	NIL
5	68/M	Post radiation necrosis–cheek	6	66Gy in 33# 3DCRT	NIL
6	61/M	Post radiation necrosis–oral cavity	12	66Gy in 33# 3DCRT	NIL
7	57/M	Post radiation necrosis–oral cavity	18	66Gy in 33# 3DCRT	NIL
8	57/M	Post radiation necrosis–oral cavity	6	66Gy in 33# 3DCRT	NIL
9	68/M	Post radiation necrosis–mandible	6	66Gy in 33# 3DCRT	NIL
10	80/M	Post radiation necrosis–oral cavity	12	66Gy in 33# 3DCRT	NIL
11	61/M	Post radiation necrosis–oral cavity	18	66Gy in 33# 3DCRT	NIL
12	36/M	Post radiation necrosis–oral cavity	24	66Gy in 33# 3DCRT	NIL
13	70/M	Post radiation necrosis–oral cavity	21	66Gy in 33# 3DCRT	NIL
14	58/M	Post radiation necrosis–cheek	24	66Gy in 33# 3DCRT	NIL
15	65/M	Post radiation necrosis–oral cavity	30	66Gy in 33# 3DCRT	Reversible myopia
16	48/M	Post radiation necrosis–oral cavity	6	66Gy in 33# 3DCRT	NIL
17	67/M	Post radiation necrosis–oral cavity	6	66Gy in 33# 3DCRT	NIL
18	65/M	Post radiation necrosis–mandible	12	66Gy in 33# 3DCRT	NIL
19	68/M	Post radiation necrosis–mandible	12	66Gy in 33# 3DCRT	NIL
20	60/ F	Post radiation necrosis–oral cavity	12	66Gy in 33# 3DCRT	NIL
21	70/M	Post radiation necrosis–cheek	20	66Gy in 33# 3DCRT	NIL
22	65/M	Post radiation necrosis–oral cavity	20	66Gy in 33# 3DCRT	NIL
23	38/M	Post radiation necrosis–oral cavity CA tongue	30 + 12 = 42	66Gy in 33# 3DCRT	NIL
24	64/M	Post radiation necrosis–oral cavity CA cheek	6	66Gy in 33# 3DCRT	NIL
25	65/M	Post radiation necrosis–oral cavity CA cheek	12	66Gy in 33# 3DCRT	NIL
26	51/M	Post radiation necrosis–oral cavity CA buccal mucosa	12	66Gy in 33# 3DCRT	NIL
27	31/M	Post radiation necrosis–CA breast	12	50Gy in 25# 3DCRT	NIL
28	42/M	Post radiation necrosis–oral cavity CA buccal mucosa	18 + 15 = 33	66Gy in 33# 3DCRT	NIL
29	62/M	Post radiation necrosis–oral cavity CA tongue	30	66Gy in 33# 3DCRT	NIL
30	72/F	Post radiation injury left leg–post sarcoma excision	30	60Gy30# 3DCRT	NIL

Gy Gray, *#3DCRT*2 Fractional 3-dimensional conformal radiotherapy

and neck cancers are dealt by plastic surgeons, these wounds are referred for final management to plastic surgeons. Hence, there is a need for plastic surgeon to know about the modalities used for healing of radiation-induced ulcers.

Following head and neck cancer irradiation, any bone and soft tissue can be undergoing radiation-induced injury. Mandible is by far the most common site for osteonecrosis because the primary arterial supply of the mandibular body is through the inferior alveolar artery, whereas the remaining bones of the head and neck regions receive blood distribution through highly redundant periosteal and muscular perforators. Radiographically, periosteal thickening and lytic destruction are common [7].. A tumour recurrence should always be excluded. Mandibular resection is necessary in 12 to 40% of patients initially treated with conservative measures without hyperbaric oxygen therapy [8].

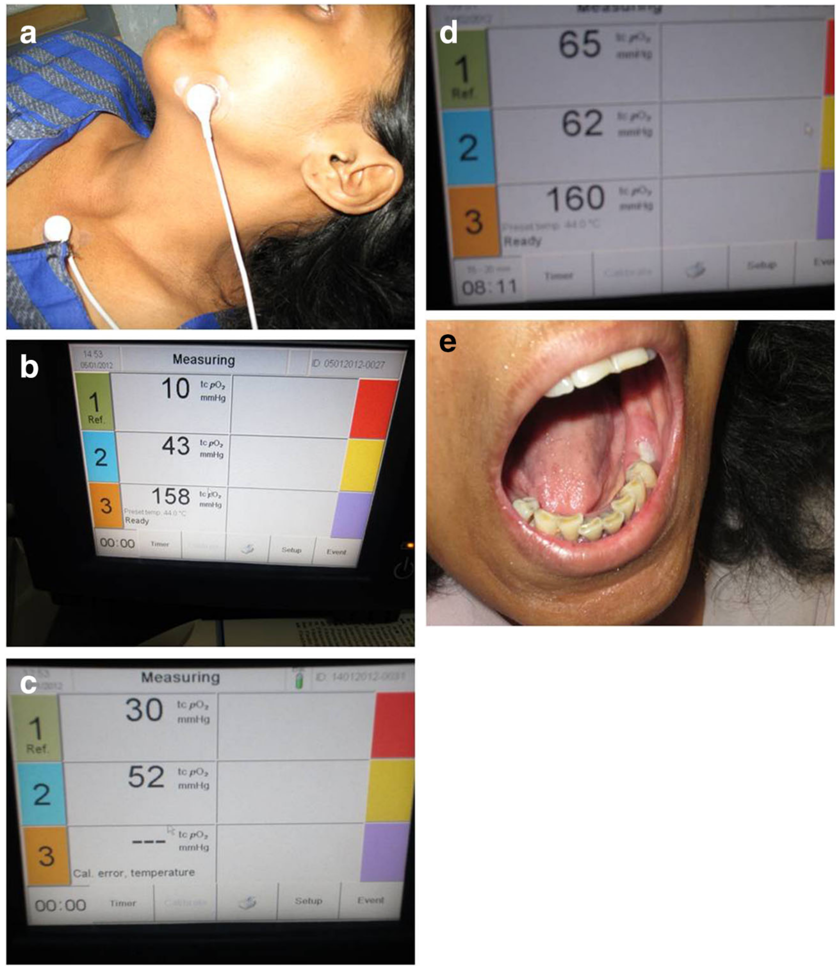

Fig. 1 **a** Transcutaneous oximetry done over the mandibular region before tooth extraction. **b** Levels of oxygen measured on admission. **c** Increasing levels of oxygen after initiation of hyperbaric therapy. **d** Oxygen level improved from 10 to 65 mmHg following 28 sessions of hyperbaric oxygen therapy. **e** Picture showing healed dental extraction region

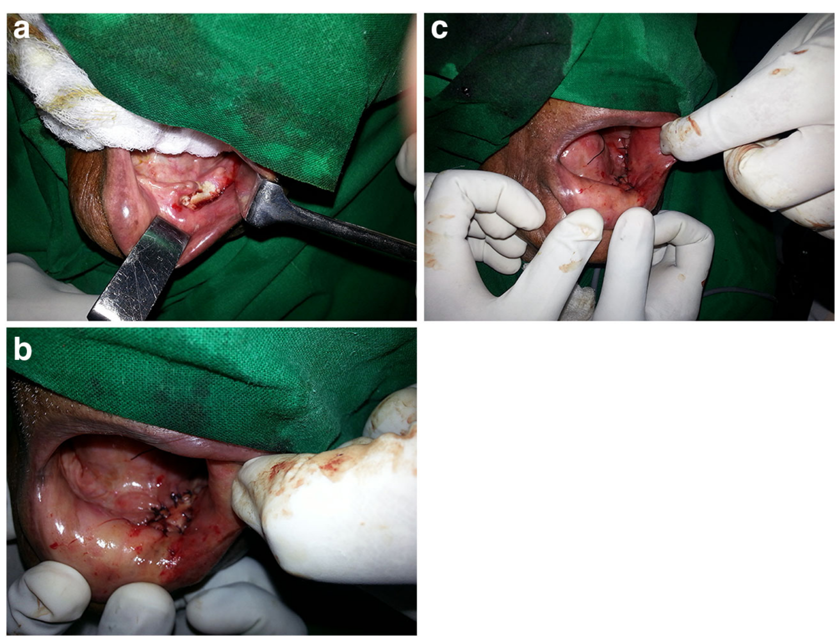

Fig. 2 **a** Picture indicating the exposed necrotic mandible following irradiation. **b** Local mucosal flap cover done after improving the tissue oxygenation by HBO. **c** Donor area closed primarily

Fig. 3 **a** Wound dehiscence in bilateral nasolabial region following nasolabial flap and maxillary osteoradionecrosis. **b** Wound debridement done following HBO sessions. **c** Local cheek rotation flap cover done. **d** Postoperative follow-up with administration of HBO for wound healing. **e** Late postoperative appearance of the healed flap

Healing of wound in the vicinity of radiated tissue may also be difficult. A simple dental extraction procedure in an irradiated mandible may cause a persisting ulceration with denuded bone.

HBO therapy has been used for several decades as an adjunct to appropriate surgery in the treatment and prophylaxis of ORN. HBO stimulates angiogenesis and increases neovascularization, cellular levels of oxygen, fibroblast and osteoblast proliferation and collagen formation in irradiated tissues. In full-dose irradiated patients, no surgery should preferably be attempted in the jaw before the first 30 HBO treatments have provided. Hyperbaric oxygen induces neovascularization of irradiated tissue, and the tissue PO2 raises to 81% of normal between 18 and 30 hyperbaric treatments [6]. Successful surgery and grafting is possible only with a PO2 of 75% of normal. Also HBO should be resumed as soon as possible after surgery.

The ORN may also progress to a fracture of the jaw requiring mandibulectomy with complex surgical reconstructive procedure. Surgical reconstructive procedure includes a faciomaxillary surgeon to extirpate necrotic bone in stage 1, who works together with the plastic surgeons for resections and reconstructive surgery in stages 2 and 3, depending on clinical severity. HBO as an adjunct in the multidisciplinary bony reconstruction procedures increases the vascular density, so that the hypoxic, acellular matrix in the post irradiated field is changed to a more normoxic situation. Pre-operative and postoperative administration of HBO together with an aggressive surgical approach has increased the salvage rate for ORN dramatically [9]. The cure rate for radionecrosis of the mandible now approaches to about 94% in those patients treated with hyperbaric oxygen [10]. The effect of hyperbaric oxygen in radiation-induced severe laryngeal necrosis, hemorrhagic radiation cystitis, colitis, and scleral necrosis are also now well recognized. Early identification of ischaemia and upfront HBOT before dental extraction is always beneficial than administering HBOT after osteoradionecrosis is already established.

Conclusion

Hyperbaric therapy is a useful adjunct for surgery in management of osteoradionecrosis and post irradiation wound and proves therapeutic in some post irradiated wound where we cannot offer surgical correction.

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