How should hyperbaric oxygen therapy be utilised in the management of osteoradionecrosis of the mandible?

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Background

Osteoradionecrosis (ORN) of the mandible is a severe non-healing condition, which involves irradiated necrotic bone becoming exposed through ulcerated skin or mucosa.[1] It usually arises 6–12 months following radiotherapy in patients with head or neck cancer.[1] Patients present with pain and trismus (spasm of jaw muscles) as the most prominent symptoms.[2]

Risk factors for mandibular ORN include previous dental extraction, oral mucositis and smoking.[3] However, the most significant risk factor is exposure to a radiation dose of greater than 60 grays (Gy). Radiation-induced injury to the inferior alveolar artery and its branches ultimately leads to ischaemic necrosis of the mandible.[4]

Hyperbaric oxygen therapy as a treatment

The Notani staging system can be used to classify the severity of ORN based on clinical and radiological findings.[5] The stage of disease ultimately determines what treatment is given. Treatment of early-disease ORN involves the use of local wound irrigation and antibiotics, whereas surgical reconstruction is often performed in more severe cases, i.e. grade III ORN **(Figure 1)**.[6]

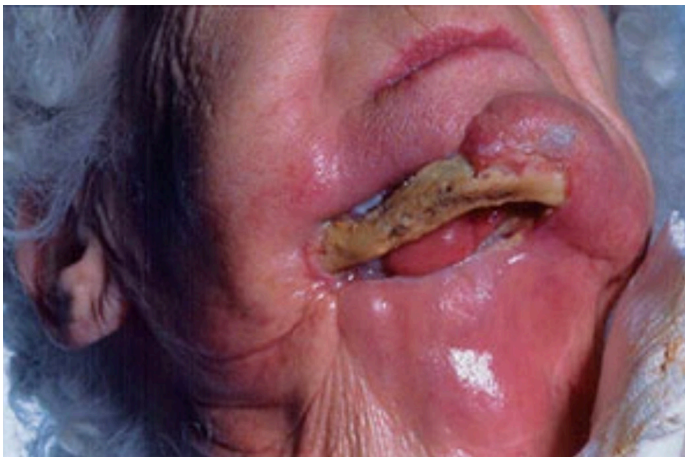

Figure 1. Grade III mandibular ORN. Image from Thomson et al[14], reprinted by permission from Springer Nature.

Hyperbaric oxygen therapy (HBOT) involves inhaling 100% oxygen at 3 atmospheres pressure in an enclosed body chamber. This results in a considerable increase in the concentration of oxygen dissolved in blood plasma (and percentage saturation of haemoglobin).[7] Despite oxygen levels returning to normal after 10 minutes of HBOT, a greater supply of oxygen reaches tissues during the session.[7] Although HBOT is utilised in all stages of ORN, the literature remains unclear as to whether HBOT is more effective when used as a standalone treatment, or as an adjunct to surgery.

Standalone treatment An unblinded randomised trial by Tobey and Kelly concluded that HBOT improved the recovery rate for patients with ORN by improving the likelihood of complete mucosal covering.[8] This is supported by a systematic review, which supported the application of HBOT for a select number of patients.[9] However, this systematic review focused more on HBOT use as prophylaxis, as opposed to treatment once ORN had developed. Moreover, the use of an unblinded trial introduces an element of bias, as patients with less severe ORN could have been favoured in the selection criteria.

A double-blind study carried out by Annane et al evaluated HBOT therapy without the use of surgery or any additional treatment methods in comparison with a placebo group. Nineteen per cent of the participants in the experimental group made a full recovery as opposed to 32% in the placebo group. This trial suggests that HBOT should not be used as a standalone treatment for mandibular ORN.[10] A limitation of this study is that HBOT was used twice daily, as opposed to once, therefore differing from standard guidelines. However, the trial was of high quality since it was double-blinded and was conducted at multiple centres.

Adjunct to surgery In contrast to standalone treatment, evidence supports the use of HBOT in conjunction with surgery. A retrospective study carried out by D'Souza et al showed that HBOT was not able to cure ORN in patients with grade II or III disease if it was used alone; however, if it was administered before or after surgery to the mandible, it had beneficial effects.[11] This is supported by a recent study demonstrating that, when used alongside adjunctive HBOT, surgical bone debridement or reconstruction resulted in significant patient recovery rates. However, early surgical intervention was essential, particularly in grade II or III ORN.[12]

Furthermore, a study by Dieleman and colleagues, found that the highest cure rate for patients with grade II and III ORN was achieved with extensive surgery (a free vascularised osteocutaneous flap) alongside HBOT.[5] However, only a small sample of 27 patients was included in this study.

It is believed that HBOT can increase the success of procedures, such as local flaps or bone grafts. A critical factor for bone-graft survival is the presence of a recipient bed that is already well vascularised and has an abundance of cells capable of osteoinduction.[6] Exposure of tissue to hyperoxic levels stimulates fibroblasts to produce collagen at the site of the wound, which then enables endothelial cells to proliferate into capillary buds.[13] The focal point of HBOT is, therefore, to enhance collagen synthesis, which will, in turn, promote neovascularisation, providing the vascular bed required for a successful bone graft. Local flaps are usually already well vascularised, so do not necessarily rely on this mechanism.[13]

Conclusion

There is little evidence to support the use of HBOT as a standalone treatment for mandibular ORN. Results for its use in grade I ORN have been inconsistent and its efficacy as a lone therapy for treating grade II and grade III ORN show little to no benefit. As far as current research goes, HBOT is best utilised as an adjuvant to a surgical procedure, as this is shown to have the greatest impact on recovery rates in patients with ORN.

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