Comparison of Australian and New Zealand referral rates for hyperbaric oxygen in oro-facial osteoradionecrosis: evidence-based, funding constraint or clinician whim?

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Abstract

(Sames C, Gorman DF, Sandiford P, Zhou L. Comparison of Australian and New Zealand referral rates for hyperbaric oxygen in oro-facial osteoradionecrosis: evidence-based, funding constraint or clinician whim? *Diving and Hyperbaric Medicine*. 2015 December;45(4):244-246.)

Aim: To compare Australian and New Zealand (NZ) rates of referral to hyperbaric units for patients with, or at risk of developing mandibular or maxillary osteoradionecrosis (ORN) due to a history of radiotherapy for oro-pharyngeal cancer.

Method: Relevant patient treatment data from all hyperbaric units in Australia and NZ were collated and analysed.

Results: The rate of referral to hyperbaric units in Australia for treatment or prophylaxis of patients with, or at risk of oro-facial ORN, was 1.7 times the rate of referral in NZ. Within Australia, there was a greater than three-fold interstate variation.

Conclusion: There is a significant referral rate difference both within Australia and between Australia and NZ for hyperbaric oxygen therapy for oro-facial ORN. Possible reasons for this difference include access to funding, logistical difficulties, clinician preference for an alternative treatment and clinician attitudes to hyperbaric oxygen.

Key words

Hyperbaric oxygen therapy; osteoradionecrosis; evidence; survey

Introduction

There is good evidence that normal tissue is damaged by radiotherapy, and that bone, especially the mandible, is vulnerable to the development of osteoradionecrosis (ORN).[1] This has been described as a defect in wound healing and the risk is increased by trauma or surgical procedures.[2–4] Once established, the requirement for both surgical debridement and adjunctive hyperbaric oxygen (HBO) is uncertain. Some of the uncertainty is likely attributable to a single randomised controlled trial (RCT) that showed that, in moderate cases, HBO alone conferred no benefit over surgery alone.[5] However, this study assessed HBO as a primary rather than adjunctive treatment; by contrast, the generally advocated, multidisciplinary Marx protocol is a combination of HBO and thorough debridement of necrotic bone.[6] In this context it is accepted that HBO does not obviate the need for complete surgical debridement.[7]

In a systematic review of the use of HBO for delayed radiation injuries, 14 published studies are cited, which review the application of HBO to ORN of the mandible.[8] Of these, one was a small RCT (12 patients) and the others were case series. All but one showed an advantage using HBO in treating existing ORN of various stages. In the study that did not show an advantage, HBO was only given post-operatively, thus supporting Marx's general principle that HBO is important prior to surgical wounding in irradiated tissues.[9] In view of reported high success rates in advanced cases of ORN using microvascular reconstruction without HBO, the weight of evidence may be moving in favour of limiting the use of HBO to moderate and mild cases.[10]

The reported incidence of ORN has varied over the decades since Marx's original study, probably due to improved surgical and radiotherapy techniques such as intensity modulated radiotherapy (IMRT). Two controlled studies comparing ORN incidence post dental extraction reported rates of 5% vs. 30% and 3% vs. 14% with or without prophylactic HBO respectively.[4,11] Several studies have shown that risk increases with radiation dosage, time since radiation, trauma (such as dental extraction) and poor oral hygiene. Spontaneous development of ORN occurs in 5–15% with older technologies, and is as low as 0–6% using newer technologies.[12–15] These lower rates have called into question the ongoing need for HBO, but they do not take account of the additional impact of dental extraction, and there are no published relevant controlled trials. Comprehensive systematic reviews have concluded that the evidence is limited and conflicting, and although HBO shows promise, better quality studies are needed.[16,17]

The practice of performing a tooth extraction or other surgery in an irradiated field without prescribing HBO is not uncommon. A UK survey showed that a third of dental and maxillofacial clinicians never prescribe HBO, and in a more recent US study comparing the attitudes of radiation oncologists and hyperbaric physicians, of the 37% of radiation oncologists and 18% of hyperbaric physicians who do not recommend HBO for prophylaxis of ORN, 52% and 38% respectively cited 'lack of evidence' as the reason.[18] Not surprisingly, a majority of both groups supported further RCTs.[19] In Denmark, most of the relevant referring clinicians considered HBO helpful in ORN but felt that the existing level of evidence was a barrier to referral.[20]

An informal review of cases referred to a New Zealand (NZ) hyperbaric unit identified a significant number of patients in whom surgery or tooth extraction was undertaken in an irradiated field without referral for prophylactic HBO. Clearly, it is possible that irradiated patients who are at risk of developing mandibular or maxillary ORN, and who might benefit from HBO as an adjunct to any dental or maxillofacial surgical procedure, may not receive such care.

The aim of this study was to determine whether there is a difference between the rates of referral in NZ and Australia, and also between the Australian states. A significant difference may imply inappropriate under or over-treatment, or preference for an alternative treatment for ORN.

Method

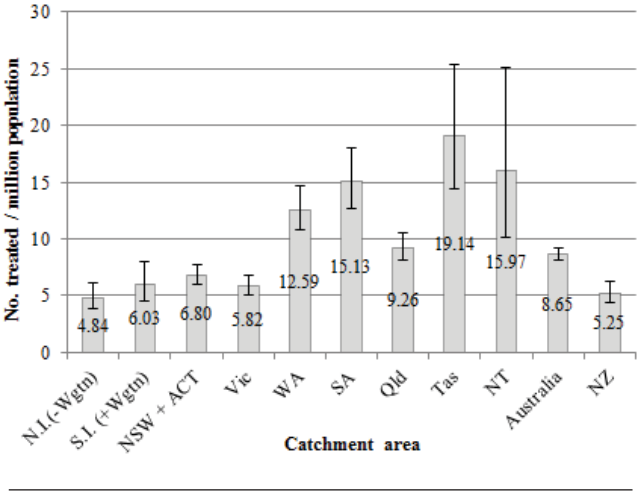
This study was approved by the Waitemata District Health Board Human Ethics Committee (reference number RM13034). Data collected from all Australian and NZ hyperbaric units by the Hyperbaric Technicians and Nurses Association between 01 July 2009 and 30 June 2014 were reviewed, and the figures relating specifically to mandibular or maxillary ORN were collated and analysed. Population estimates published on the websites of the Australian Bureau of Statistics and Statistics New Zealand were used to derive referral numbers per million of population from the relevant catchment areas. Because the raw data set was anonymised, comprising only the numbers of patients treated at the units, analysis of patient demographics was not possible.

The accuracy of the comparisons between Australia and NZ are based on the assumption that the age/sex distribution of the Australian and NZ populations is similar. Comparison between Australian states also depends on the assumption that patients accessed HBO in their own catchment area, apart from those in the Australian Capital Territory (ACT) who accessed HBO at New South Wales (NSW) units. The 95% confidence limits were calculated assuming a Poisson distribution of HBO intervention counts and error-free population estimates. The significance of the variations in referral rates between Australian states and between Australia and NZ was tested using the Poisson regression model. Statistical analysis was undertaken using SAS9.4.

Results

The mean rate of referral to hyperbaric units in Australia for treatment or prophylaxis of patients with, or at risk of oro-facial ORN was significantly higher than the rate in New Zealand (rate ratio 1.7, 95% confidence limits (CI): 1.4, 2.0). There was also significant variation in referral rates between Australian states, with Victoria having a significantly lower rate, and Tasmania a significantly higher rate than the rest of Australia. Figure 1 shows the area-specific mean HBO referral rates with 95% CIs. In New Zealand, patients resident in the Wellington (Wtgn) catchment area (in the south of the North Island) are referred to the Christchurch hyperbaric unit (in the South Island) for proximity reasons, hence the categories N.I.(-Wgtn) and S.I.(+Wgtn) in Figure 1.

Figure 1
Mean numbers of patients with osteoradionecrosis of the jaw treated with hyperbaric oxygen per million population 01 July 2009–30 June 2014 for each Australian state and the two regions of New Zealand; bars represent 95% confidence intervals



Discussion

Lack of a specific ICD-10 code for oro-facial ORN made it impossible to estimate hospital-based incidence or treatment rates in either Australia or New Zealand, but it seems unlikely that these would vary sufficiently to account for such significantly different referral rates on purely clinical grounds. The impact of logistical issues such as travel, accommodation and the significant time commitment cannot be ignored, and it is likely that some patients will decline treatment if they have to be away from home for six weeks. Clinician preference for the recently introduced treatment of ORN with a combination of pentoxifylline, vitamin E and clodronate (Pentoclo) over 1–2 years in some regions, but not others, could contribute to regional variation. An audit of treatment preference among the relevant clinicians would help clarify this matter.

Other possible reasons for variation in referral rates are; mode of radiation delivery (IMRT being the most likely, but not invariable, and data not available for this study), access to funding, and clinician attitudes to the use of HBO for ORN. In Australia, funding for HBO in oro-facial ORN is readily available from three sources in all states, namely; state health departments, Medicare and private health insurance. Thus, the three-fold interstate referral variation is more likely due to clinician experience with, or attitude to, HBO use for ORN. There is no reason to believe that the attitudes of Australian or NZ clinicians are likely to differ from those in the UK, USA or Denmark, previously mentioned.[18–20]

In NZ, the only funding source until very recently has been via individual District Health Boards, and this has certainly been an impediment to HBO access for some patients. The

lower referral rate in NZ cannot, therefore, be attributed solely to clinician attitude. With the recent adoption of HBO funding in NZ by the National Health Board, funding barriers to referral have been removed, so more accurate comparisons with Australian referral rates are likely in the future.

We accept that a limitation of this audit is due to the difficulty in collecting accurate data from all of the hyperbaric units. In this regard, it was unfortunate that a number of small, privately operated hyperbaric units in New South Wales and Victoria declined to participate in this study. Higher referral numbers in NSW and Victoria would reduce the inter-state variations in Australia, but they would increase the variation between Australia and NZ. We also accept that the above data refer to 'treatment' rates, but we have chosen to use this as a surrogate for 'referral' rates, on the basis that referral for ORN is exceedingly unlikely to result in refusal to treat.

If clinician attitude is the reason for the apparent under-use of HBO in oro-facial ORN, this is understandable on the basis of conflicting reports and paucity of high-grade evidence. Moreover, verification of HBO efficacy in ORN treatment requires further high-quality research, and this will in turn depend on improvements in the ICD coding system so that patients can be identified from clinical databases.

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Conflict of interest: nil

Submitted: 10 April 2015; revised 02 October 2015
Accepted: 15 October 2015

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