

# **Hyperbaric oxygen treatment protocols for mandibular osteoradionecrosis.**

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Wreford-Brown CE, Hampson NB. Hyperbaric oxygen treatment protocols for mandibular osteoradionecrosis. *Undersea Hyperb Med* 2003; 30(3): 175-179 - To determine hyperbaric oxygen (HBO<sub>2</sub>) treatment practices for osteoradionecrosis (ORN) of the mandible in North America, we surveyed hyperbaric facilities listed in the 1998 UHMS Chamber Directory. A survey response rate of 99.7% was achieved. Among the 316 facilities listed, 280 treat or would treat mandibular ORN with HBO<sub>2</sub>. Twelve different hyperbaric treatment protocols for the condition were reported. Approximately three-quarters of facilities utilize a protocol administering 90 minutes of 100% oxygen breathing at a treatment pressure of 2.4-2.5 atmospheres absolute (atm abs). The remaining one-quarter of facilities apply alternate hyperbaric treatment protocols. In summary, mandibular ORN is commonly treated at North American hyperbaric facilities but there is a lack of uniformity with regard to the protocol utilized for hyperbaric oxygen administration. There are no clinical data to support that any one treatment protocol is superior in outcome to any other.

*Osteoradionecrosis, hyperbaric oxygen, protocols*

## **INTRODUCTION**

Hyperbaric oxygen (HBO<sub>2</sub>) therapy is often recommended and used for treatment of significant radiation injury to bone and soft tissue. Radiation doses greater than 5,000 centi-Gray can cause progressive radiation fibrosis and capillary loss over time (1). The mandible, a dense, poorly vascularised bone is particularly vulnerable to radiation in the head and neck area. The high partial pressure of oxygen (O<sub>2</sub>) achieved with HBO<sub>2</sub> has been demonstrated by Marx and co-workers to stimulate angiogenesis and fibroplasia in affected tissue (2, 3).

A variety of different hyperbaric protocols are mentioned in the literature for treatment of chronic radiation tissue injury (4, 5, 6). These describe use of treatment pressures ranging from 2.0 to 3.0 atmospheres absolute (atm abs). As animal studies have shown that angiogenesis in irradiated tissue is oxygen dose dependent (3, 7), a wide range of therapeutic pressures has the potential to affect clinical outcomes from HBO<sub>2</sub> therapy. The purpose of this study was to determine how radiation injury to the mandible is treated at North American HBO<sub>2</sub> facilities.

## **METHODS**

A mail survey was sent in 1999 to the nurse managers of all clinical hyperbaric chamber facilities in the United States and Puerto Rico listed in the 1998 Undersea and Hyperbaric Medical Society (UHMS) chamber directory (8). Subsequent mailings, telephone calls and electronic mail contacts were performed as necessary to achieve a high response rate. Excluded from the study were facilities that had closed since publication of the directory.

The survey comprised a questionnaire inquiring about each facility's current practice with regard to the hyperbaric treatment of osteoradionecrosis (ORN) of the mandible. Specific information was collected regarding type of hyperbaric chamber used, maximum treatment pressure, minutes of 100% oxygen administered at treatment pressure, and number of treatments administered per patient per day. Simple descriptive statistics were used to report results.

## **RESULTS**

Of the 316 hyperbaric chamber facilities listed in the 1998 UHMS directory, 315 responded to the survey, resulting in a 99.7% response rate. One facility declined to share treatment data. At the time of the survey, 7 facilities had closed since the time of directory publication. Of the remaining 308, a total of 280 hyperbaric facilities (91%) do treat or would treat ORN of the mandible. These 280 comprised the study group. They included 65 multiplace chamber facilities, 210 monoplace, and 5 facilities with both types of chamber.

A total of 12 different treatment protocols for mandibular ORN were reported by the 280 treating facilities (Table 1). The maximum treatment pressure utilized per protocol ranged from 1.9 to 2.5 atm abs. The time breathing HBO<sub>2</sub> varied from 80 to 120 minutes. The pressure/time combinations most commonly reported were 2.4 atm abs/90 minutes (134 facilities) and 2.5 atm abs/90 minutes (71 facilities). Combined, these accounted for 73% of treating facilities. Two facilities reported protocols that use more than one oxygen breathing pressure in the same treatment profile. Among the 278 treating facilities using a single treatment pressure, 1 facility reported treatment at 1.9 atm abs, 61 at 2.0 atm abs, 3 at 2.2 atm abs, 138 at 2.4 atm abs, and 75 at 2.5 atm abs (Figure 1).

Of the 280 treating chamber facilities in the study, 1 reported oxygen administration at the therapeutic pressure for 70-80 minutes, 1 for 85 minutes, 258 (92%) for 90 minutes, 19 for 120 minutes, and 1 for 140 minutes.

Frequency of HBO<sub>2</sub> treatment also varied among facilities. Within the treating group, 253 (90%) treat only once daily, while the remaining 27 will consider twice daily treatment. The latter is usually done under specific circumstances, e.g. strong patient preference, managing physician choice, or if treating a hospital inpatient.

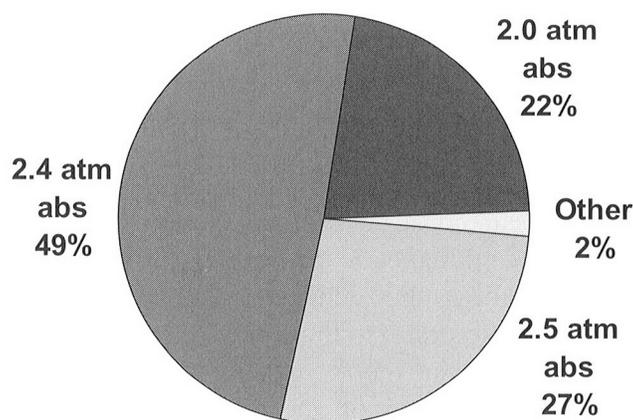
Of the hyperbaric facilities that treat or would treat established ORN, 246 (87%) use or would use perioperative HBO<sub>2</sub> for treatment of ORN when dental extractions are planned in a previously irradiated jaw.

**Table 1. Hyperbaric protocols for osteoradionecrosis.**

Protocol	Facilities	Pressure #1 (atm abs)	Oxygen Time #1 (min)	Pressure #2 (atm abs)	Oxygen Time #2 (min)
1	1	2.4	70-80 <sup>1</sup>		
2	1	1.9	90		
3	48	2.0	90		
4	1	2.5	30	2.0	60
5	3	2.2	90		
6	1	2.4	85		
7	134	2.4	90		
8	71	2.5	90		
9	1	2.4	80	0.6	60
10	13	2.0	120		
11	2	2.4	120		
12	4	2.5	120		
Total	280				

<sup>1</sup>Depends on chamber pressurization time

**Figure 1. Percentage of facilities treating mandibular osteoradionecrosis at various maximum pressures.**



## DISCUSSION

In this study, 12 different protocols were reported to be utilized by North American hyperbaric facilities for treatment of the same pathologic condition, established mandibular osteoradionecrosis. While most utilize the same protocol (2.4-2.5 atm abs pressure with 90 minutes of oxygen administration), fully one-quarter of facilities apply alternate hyperbaric treatment protocols. While no controlled human trials exist to guide protocol selection, results of both controlled animal studies and clinical case series are available. Ehler and co-workers

demonstrated in rabbits that a pressure-response curve exists when treating radiation injury (7). They constructed a “dose response curve” for angiogenesis by administering HBO<sub>2</sub> at various partial pressures to previously irradiated experimental animals. In those studies, oxygen administration time was constant at 90 minutes. As such, the oxygen dose gradation was achieved solely by varying treatment pressure. An increasing effect on angiogenesis was demonstrated as treatment pressure was increased from 1.5 to 3.0 atm abs. Despite the fact that greater angiogenesis was stimulated by 3.0 atm abs treatment than 2.5 atm abs, the investigators recommended the use of 2.5 atm abs in order to balance the benefit of HBO<sub>2</sub> with an acceptable level of treatment risk for clinical oxygen toxicity. These conclusions are all drawn from animal studies, however, and there are no confirming data from clinical trials.

In the present survey, facilities reported use of hyperbaric treatment pressures as low as 1.9 atm abs for mandibular ORN. According to Ehler’s experimentally derived dose response curve, this pressure would be expected to stimulate only approximately 60% of the capillary density that would be achieved by treatment at 2.5 atm abs (7). It should be recognized that Ehler’s data were derived in animals. Whether the same relationships are directly applicable to humans is currently unknown.

As noted above, extensive clinical experience treating mandibular ORN with HBO<sub>2</sub> has been reported. The largest published experience has been that of Marx and co-workers. In a 1988 update of their work, they reported a 100% clinical success rate treating 268 cases of mandibular ORN when utilizing a hyperbaric protocol administering 90 minutes of oxygen at 2.4 atm abs per treatment, in conjunction with appropriate surgery (2). Other more recent series have reported lower success rates with the same hyperbaric protocol (9, 10), possibly related to differing patient populations and/or surgical technique.

The UHMS Hyperbaric Oxygen Therapy Committee recommends that radiation injury be treated daily at 2.0-2.5 atm abs with 90-120 minutes of 100% oxygen administration (11). A more specific protocol is not indicated. The pressure range suggested likely relates at least in part to historical practice differences between monoplace and multiplace hyperbaric chambers. In monoplace chambers not equipped for breaks of air breathing, continuous oxygen administration is often performed at 2.0 atm abs to minimize risk of central nervous system oxygen toxicity (12). While one can construct protocols over the range of UHMS recommended pressures, it is not known whether therapeutic equivalency can be achieved by longer oxygen administration at a pressure just above that which is minimally effective. The most common protocol used in the United States according to this study is 2.4 atm abs. Animal studies have not been reported that vary time rather than the oxygen treatment pressure to change the oxygen dose. That normobaric oxygen administration in an experimental model of chronic radiation injury confers no benefit over air breathing suggests that a certain minimal PO<sub>2</sub> must be achieved for therapeutic benefit to occur (3).

In summary, mandibular osteoradionecrosis is treated in North America with a range of different HBO<sub>2</sub> protocols that apply treatment pressures of 1.9 to 2.5 atm abs. Animal data suggest that angiogenesis in irradiated tissue is greater as pressure increases over this range. Clinical experience in the treatment of human mandibular ORN has been very successful with HBO<sub>2</sub> delivered at 2.4 atm abs. Controlled clinical trials are needed to compare the efficacy of the different HBO<sub>2</sub> doses delivered by various protocols.

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