The Use of Hyperbaric Oxygen Therapy in Head-and-Neck Conditions

Syed Nabil, Rifqah Nordin, Firdaus Hariri1, Ahmad Fahmi Mohamad Bustaman2, Sharifah Azlin Juliana Syed Zainal3, Divya Panicker3, Abdul Jabar Nazimi

Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, The National University of Malaysia, Bangi, 1Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, University Malaya, Departments of 2Oral and Maxillofacial Surgery and 3Hyperbaric Medicine, Hospital Angkatan Tentera Tuanku Mizan, Ministry of Defence, Kuala Lumpur, Malaysia

Address for correspondence: Dr. Syed Nabil, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, The National University of Malaysia, Jalan Raja Muda Abdul Aziz, 50300 Kuala Lumpur, Malaysia. E-mail: syednabil@ppukm.ukm.edu.my

ABSTRACT

Introduction: Hyperbaric oxygen therapy (HBOT) has been suggested to be beneficial in managing compromised acute and chronic wounds. To shed some light on its effectiveness in head-and-neck wounds, a retrospective review on the use of HBOT was done. Materials and Methods: The medical records of patients receiving HBOT for head-and-neck conditions were reviewed. The demographics and clinical data were collected. Results: Seventeen patients were identified. Four major indications for therapy were identified being osteoradionecrosis (ORN) treatment, ORN prophylaxis, treatment of compromised flaps/grafts, and treatment of medication-related osteonecrosis of the jaw. Favorable outcome following HBOT was seen in 77% of patients. In the treatment of ORN, 56% cases treated were successful. In the remaining groups, 100% success rates were obtained. The majority of patients had HBOT as an adjunctive treatment. HBOT as an adjunct was successful in 71% of patients, while prophylactic HBOT were successful in all patients. Complications including ear barotrauma and sinus squeeze were seen in 24% of patients. Conclusions: HBOT can be successfully used in various head-and-neck conditions, especially when used in cases with compromised flaps/graff or ORN prophylaxis. It is well tolerated and thus provides a valid adjunctive therapy in the management of tissue with compromised healing capability in the head-and-neck region.

Key words: Bisphosphonate, flaps, head and neck, hyperbaric oxygen therapy, osteoradionecrosis

INTRODUCTION

With the recent emphasis on evidence-based medicine, hyperbaric oxygen therapy (HBOT) has been put on the spotlight once again. Once labeled as “a therapy in search of diseases,” it is now finding its way as a valid contemporary therapy.1 Hyperbaric oxygen therapy (HBOT) is defined by the Undersea and Hyperbaric Medical Society (UHMS) as a treatment in which a patient intermittently breathes 100% oxygen while the treatment chamber is pressurized to a pressure greater than sea level (1 atmosphere absolute [ATA]).2

The physiological effect of HBOT is hyperoxia in blood and tissues. Human body tissue oxygen requirement to maintain normal cellular metabolism at rest is about 60 ml/l of blood flow.3 At atmospheric pressure, almost all the oxygen in our body is transported by being bound to hemoglobin with very minimal amount carried in plasma (around 3 ml/L). However, breathing 100% oxygen at 3 ATA as in HBOT allows the delivery of 60 ml oxygen per liter of blood dissolved in plasma, which is sufficient to support resting tissues without a contribution from hemoglobin-bounded oxygen.3 This would allow the oxygen in plasma alone to oxygenate tissue when there is poor perfusion or when hemoglobin is compromised, such as in carbon monoxide poisoning and severe anemia.

Based on this understanding, HBOT has been recommended and used for a wide range of medical conditions, with varying levels of evidence. It has been suggested to be used in 14 conditions by the UHMS.2 However, the scientific evidence supporting its use is strong mainly in decompression sickness, carbon monoxide poisoning, arterial gas embolism (AGE), clostridial myonecrosis, compromised grafts/grafts, and osteoradionecrosis (ORN) prevention.4 In the head-and-neck region, the possible application of HBOT includes delayed radiation injury (soft tissue and bony necrosis), refractory osteomyelitis, necrotizing soft-tissue infections, compromised skin...
flaps and grafts, and thermal burns.[2] The pattern of use of HBOT for head-and-neck conditions is not clear. This study aims to review the use of HBOT in the management of head-and-neck conditions in the main HBOT center in Malaysia.

**MATERIALS AND METHODS**

The list of patients who had HBOT in the hyperbaric oxygen unit at a main referral center was reviewed over 3-year period. The facility which consists of a multiple hyperbaric oxygen chamber is capable of housing several patients and a therapist during a dive. Patients who had HBOT for head-and-neck conditions were identified. These patient medical records were then reviewed and formed the sample of this review. The demographic and clinical data were collected. Demographic data included age of patient, gender, race, and source of referral, i.e., the specialty involved. Clinical data collected meanwhile consisted of the diagnosis, clinical presentations, HBOT protocol used, adjunctive treatment received, outcome of treatment, complications, and patients’ tolerance.

The identified patients were then divided based on the indication for the HBOT. Further assessment was also done to stratify the intent of the therapy either as an adjunctive treatment or prophylactic purposes. Adjunctive treatment for the purpose of this study refers to HBOT that was carried out in combination with other treatments such as daily dressings, sequestrectomies, curettage, or radical surgery including resection and reconstruction of the jaw. Prophylactic meanwhile refers to HBOT used in a patient without any pathology at the time of therapy with the intention to prevent future occurrences of any head-and-neck pathology at risk. The outcomes of HBOT were graded as (1) successful and (2) failed. The treatment outcome is labeled “successful” when a positive response to therapy is seen, i.e., complete resolution or significant resolution of symptoms or clinical signs in curative intent and complete healing in preventive intent, while “failed” is in cases where the symptoms/signs persisted in adjunctive HBOT or there unhealed wound in preventive intent. Data collection was recorded in a standardized pro forma form and later was transferred to Microsoft Excel® for tabulation.

**RESULTS**

In total, 17 patients with head-and-neck conditions received HBOT during the study period [Table 1]. There were 12 males and 5 females with ages ranged from 29 to 76 years (mean age: 58.4 years). There was mixed racial distribution consisting of Chinese (8), Malays (6), and Indians (3).

Four main indications for referral were identified [Table 1]. These were for (1) ORN treatment; (2) ORN prophylaxis prior to dental extraction; (3) treatment of delayed wound healing/hypoxic wounds; and (4) treatment of bisphosphonate-related osteonecrosis. For the treatment of ORN (Group 1), it consists of nine patients between the ages of 44 and 76 years. There were six males and three females in this group. Group 2 consisted of three patients ranging from the age of 57 years to 62 years who were all males. Group 3 had four patients with age ranging from 29 years to 71 years. Three-quarter of them were male. One patient, a female aged 35 years had undergone HBOT of the treatment on medication-related osteonecrosis of the jaw (MRONJ).

Of the 17 patients reviewed in this study, the majority of referrals were from the Oral and Maxillofacial Surgery (OMFS) specialty and only one each was from the Plastic and Reconstructive Surgery (PRS) and Otorhinolaryngology (ORL) specialty. All the referrals related to ORN and MRONJ (Group 1, 2, and 4) were from the OMFS specialty.

In the present study, overall, 76.5% of the cases were successfully treated with HBO, while 23.5% failed due to persistence/worsening of the condition [Table 2]. Looking at specific indications for treatment, all failures (four cases) occurred in patients undergoing HBOT for the treatment of ORN (Group 1). In the remaining groups (Group 2, 3, and 4), a 100% success rate was obtained following HBOT.

Of the 17 patients, majority (14 patients) received HBOT as adjunctive treatment, while prophylactic treatment was received by three patients [Table 3]. When HBOT was used as an adjunct, successful treatment was seen in 71% of the patients. Prophylaxis intent HBOT was successful in all patients.

The Marx Protocol was generally used as a guide for the management of patients with ORN treatment or prevention.[3] However, due to variations in patients' compliance and tolerance to treatment, some deviation from the protocol occurred in certain cases [Table 1]. In other indications (Group 3 and 4), variations of sessions received can be seen. In total, 606 HBOT sessions were done among all 17 patients. The mean sessions of HBOT received in this sample were 35.7 sessions. The mean number of sessions for each group was 43, 33, 22, and 30, respectively, for Group 1, 2, 3, and 4.

Only one patient with ORN of the mandible had an intolerance to treatment with presentation of severe ear pain during the first dive of HBOT. Nevertheless, this did not recur and the patient managed to complete 30 sessions of HBOT before sequestrectomy and 10 sessions postoperatively. Four
<table>
<thead>
<tr>
<th>Number</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>From</th>
<th>Indication</th>
<th>Treatment</th>
<th>HBOT protocol</th>
<th>Outcome</th>
<th>Patient’s tolerance</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>Male</td>
<td>I</td>
<td>OMFS</td>
<td>ORN of the right mandible</td>
<td>Adjunctive with sequestrectomy</td>
<td>2.4 ATA; 28 sessions preoperative; 10 sessions postoperative</td>
<td>Failed - ORN persisted</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
<td>Female</td>
<td>M</td>
<td>OMFS</td>
<td>ORN of the mandible bilaterally</td>
<td>Adjunctive with sequestrectomy</td>
<td>2.4 ATA, 30 sessions preoperative; 10 sessions postoperative</td>
<td>Failed - ORN progressed</td>
<td>First session abandoned</td>
<td>Middle ear barotrauma</td>
</tr>
<tr>
<td>3</td>
<td>76</td>
<td>Male</td>
<td>M</td>
<td>OMFS</td>
<td>ORN of the left mandible</td>
<td>Adjunctive with sequestrectomy</td>
<td>2.4 ATA, 30 sessions preoperative; 20 sessions postoperative</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Middle ear barotrauma and Sinus squeeze barotrauma</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>Male</td>
<td>C</td>
<td>OMFS</td>
<td>ORN of the left mandible</td>
<td>Adjunctive with sequestrectomy</td>
<td>2.4 ATA, 30 sessions preoperative; 20 sessions postoperative</td>
<td>Failed - ORN persisted</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>5</td>
<td>71</td>
<td>Female</td>
<td>C</td>
<td>OMFS</td>
<td>ORN of the left mandible</td>
<td>Adjunctive with marginal resection of left mandible</td>
<td>2.4 ATA, 30 sessions</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>6</td>
<td>71</td>
<td>Female</td>
<td>I</td>
<td>OMFS</td>
<td>ORN of left mandible</td>
<td>Adjunctive with sequestrectomy</td>
<td>2.4 ATA, 30 sessions</td>
<td>Failed - ORN persisted</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>7</td>
<td>59</td>
<td>Male</td>
<td>C</td>
<td>OMFS</td>
<td>ORN of the maxilla with OAF</td>
<td>Adjunctive with surgical debridement and local flap</td>
<td>2.4 ATA, 30 sessions preoperative; 10 sessions postoperative</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>Male</td>
<td>M</td>
<td>OMFS</td>
<td>ORN of the right mandible</td>
<td>Adjunctive with segmental resection of right mandible</td>
<td>2.4 ATA, 30 sessions preoperative; 20 sessions postoperative</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Middle ear barotrauma</td>
</tr>
<tr>
<td>9</td>
<td>51</td>
<td>Male</td>
<td>M</td>
<td>OMFS</td>
<td>ORN of the anterior mandible</td>
<td>Adjunctive with segmental resection of anterior mandible</td>
<td>2.4 ATA, 30 sessions preoperative; 20 sessions postoperative</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>10</td>
<td>62</td>
<td>Male</td>
<td>C</td>
<td>OMFS</td>
<td>Prevention of ORN in Postirradiation dental extraction</td>
<td>Preventive</td>
<td>2.4 ATA, 30 sessions preextraction; 10 sessions postextraction</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>11</td>
<td>61</td>
<td>Male</td>
<td>M</td>
<td>OMFS</td>
<td>Prevention of ORN in Postirradiation dental extraction</td>
<td>Preventive</td>
<td>2.4 ATA, 20 sessions preextraction; 10 sessions postextraction</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>Male</td>
<td>C</td>
<td>OMFS</td>
<td>Prevention of ORN in Postirradiation dental extraction</td>
<td>Preventive</td>
<td>2.4 ATA, 20 sessions preextraction; 10 sessions postextraction</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Middle ear barotrauma</td>
</tr>
<tr>
<td>13</td>
<td>68</td>
<td>Male</td>
<td>C</td>
<td>PRS</td>
<td>Compromised grafts/flaps - postsurgical radial forearm free flap</td>
<td>Adjunctive with daily dressing</td>
<td>2.4 ATA, 29 sessions</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>14</td>
<td>71</td>
<td>Female</td>
<td>M</td>
<td>ORL</td>
<td>Compromised grafts/flaps - postsurgery split skin graft following necrotizing fascitis of the left neck</td>
<td>Adjunctive with daily dressing</td>
<td>2.4 ATA, 15 sessions</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
<tr>
<td>15</td>
<td>49</td>
<td>Male</td>
<td>I</td>
<td>OMFS</td>
<td>Compromised grafts/flaps - postsurgical right mandible resection and reconstruction for ameloblastoma</td>
<td>Adjunctive with daily dressing</td>
<td>2.4 ATA, 14 sessions</td>
<td>Success - wound healed</td>
<td>No complaint</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Contd...
patients (24%) developed HBOT-related complications. All had middle ear barotrauma with one of them also had symptoms of sinus squeeze.

**DISCUSSION**

HBOT indication of use in the head-and-neck region is related mainly to its ability to increase oxygen partial pressure in tissues. These head-and-neck conditions subjected to HBOT are mainly compromised tissue either secondary to radiation or poor vascularity. The increase in oxygen partial pressure causes cellular effects including improved neovascularization and improving postischemic tissue survival by diminishing inflammatory responses. In our study, most of the cases referred for HBOT fall under two indication listed by UHMS namely for (1) delayed radiation injuries and (2) compromised grafts and flaps. The only case which was given HBOT not meeting the indications listed by UHMS is for the MRONJ case (Group 4). The idea of HBOT for treating MRONJ however is not novel with previous study which has attempted to prove its efficacy in such condition. The evidence supporting HBOT use for delayed radiation injuries meanwhile is rather extensive with improved outcomes seen with its use. The use in compromised grafts and flaps is also quite establishing.

What is also apparent from this study is the rather low number of cases that had undergone HBOT for head-and-neck conditions, with an average of six cases per year. The hyperbaric oxygen unit in this study is the main referral center for HBOT in Malaysia, being one of two public hospitals offering HBOT in West Malaysia. This highlights the limitation of HBOT in developing countries, which is its accessibility to the patients, not only in regard
to financial factor but also logistically. A patient usually would need on average 30 sessions which indicate the need to make a visit to the center 30 times.\cite{10} Furthermore, the treatment takes almost 2 h per sessions; thus, it is a significant effort.\cite{10} Taking into consideration of limited availability, most patients had to travel couple of hours just to go to these centers.

From our study, there were 12 males and 5 females with a mean age of 58.4 years. Thirteen of 17 patients in this study have had oro-pharyngeal malignancy. With these patients forming the bulk of our study population, our sample demographics are consistent with the studies on head-and-neck squamous cell carcinoma which is more prevalent among males and in persons of more than 60 years old.\cite{11}

This study also found that most of the patients who received HBOT were related to ORN either as a treatment for established ORN or as prophylaxis to prevent ORN prior to dental extraction. HBOT was first suggested for the treatment of ORN in 1973.\cite{12} Later in a landmark study by Marx et al., HBOT was shown to be effective in preventing ORN in the irradiated head-and-neck patients undergoing dental extraction.\cite{5} HBOT effectiveness in preventing ORN in dental extraction is further supported by a pooled data indicating reduced risk of ORN when HBOT is used versus antibiotics.\cite{13} Our study, although in a small sample size, further substantiate this with all of the patient undergoing preventive HBOT had not developed ORN. This and previous studies suggested that HBOTs are beneficial for preventing ORN, although a more recent study suggests otherwise.\cite{14} In regard to treating ORN, its effectiveness is still not clear. Annane et al. found that there were no benefits of HBOT in treating overt ORN.\cite{15} Others found clear benefits of HBOT in treating ORN.\cite{16} This study similarly found that HBOTs do not clearly provide benefits in treating ORN. A possible explanation for the lack of success is probably that HBOT is effective only for the early stages of ORN.\cite{17} In our study, no data on the stage of ORN were able to be obtained from the records; thus, we could not explore further on the cases that had a failed outcome. Also, the lack of success in treating ORN is possibly linked to the limited accessibility to get HBOT, which could cause clinicians to only refer cases that are in advance stage or had failed initial treatment thus introducing bias of having mostly severe cases in this sample.

The head and neck is a complex region with multiple specialties involved in managing pathology in this anatomical area including neurology, neurosurgery, OMFS, ORL, PRS, and ophthalmology. When assess together with the 14 indications listed by UHMS, condition relating to the head-and-neck region mainly involves pathology treated by OMFS, ORL, and PRS specialty. Hence, it is not surprising to see all these specialties utilizing HBOT as part of their management of patients. Looking closely to the conditions, a clear pattern can be seen with all compromised bone tissues were referred from OMFS, while compromised soft-tissue flaps/grafts were from ORL/PRS, fitting into the bulk of work done by these respective specialties.

In general, for ORN prevention or treatment, the Marx Protocol is adhered to as a guide for the amount of sessions needed. The general rule for prevention of ORN is for the patient to undergo 20 sessions before a procedure with risk of developing ORN such as dental extraction and another 10 session after that procedure (20/10 protocol). For treatment of establish ORN the patient would need 30 sessions before the surgical treatment for ORN such as sequestrectomy and another 10 sessions after that surgery (30/10 protocol).\cite{18} However, due to variations in patients’ compliance and tolerance to the treatment, it is possible to have variation in the total sessions received. Apart from the protocol for ORN, there is no establish guide on the total treatment duration prescribed, both in terms of cumulative time or number of sessions.\cite{19} However, general rule is that acute injuries should receive 15 sessions, while chronic wound should receive 30 sessions.\cite{19} Our study seems to somewhat fit this general rule, with acute wound (compromised flap/graft healing) received a minimum of 14 sessions. The MRONJ case meanwhile received a total of 30 sessions divided evenly pre and post procedure. There are no exact guidelines for MRONJ, but a previous study by Freiberger et al. used 40 sessions in its study.\cite{7}

There are several possible complications of HBOT which include middle ear barotrauma, sinus barotrauma/squeeze, tooth barotrauma/squeeze, claustrophobia, pulmonary barotrauma (pneumomediastinum, subcutaneous emphysema, intrapulmonary hemorrhage, and pneumothorax), AGE, central nervous system/pulmonary oxygen toxicity, hyperoxic myopia, and cataract.\cite{20,22} Among those complications, serious complications such as oxygen toxicity, AGE, and pneumothorax are extremely rare.\cite{22} In our study similarly, no serious complication was seen. Only two minor complications were seen in four cases, which were middle ear barotrauma and sinus squeeze. Expectedly, these two complications are the most frequent complications reported by the previous studies.\cite{21,22} While not serious, minor complications are common and may influence the tolerance and compliance of the patient to HBOT. In a study by Ambiru et al., 4% of patients in their center had discontinued HBOT because
of these problems.[21] In the current study, although there was one patient who could not tolerate the first session due to middle ear barotrauma, she subsequently able to continue the rest of the sessions without issues. None in our series of patients had an intolerance to HBOT due to complications.

The main limitation of this study is the limited number of patients undergoing HBOT. Due to the small sample size, we were not able to satisfactorily draw a firm conclusion on the effectiveness of HBOT in treating head and neck conditions such as ORN or compromised grafts/flaps. This however highlights the infrequent use of HBOT for head-and-neck conditions. The low incidence of ORN and compromised graft/flaps is also a contributing factor to the low usage of HBOT as an adjunct. For prophylaxis HBOT, although there is a lot of potential case, the accessibility is a limiting factor.

CONCLUSION

In summary, our findings are consistent with the results of previous studies which found that HBOT can be successfully used in various head-and-neck conditions. Therefore, HBOT is a valid treatment option in the management of indicated conditions in the head-and-neck region. We found HBOT to be a safe treatment with minimal complications, with its biggest limitation being its accessibility, especially in developing countries.

Acknowledgment

The authors would like to than Dr. Annie Lem Mei Sian and Dr. Lim Tiong Boon who contributed in the data collection in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Disclosure

This material has never been published and is not currently under evaluation in any other peer reviewed publication.

Ethical approval

The permission was taken from Institutional Ethics Committee prior to starting the project. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

REFERENCES