Letters to the Editor

Malignant otitis externa: experience with hyperbaric oxygen therapy

Dear Editor,

I have read with great interest the recently published series of patients treated with hyperbaric oxygen therapy (HBOT) for malignant otitis externa (MOE).[1] I agree that the treatment of this disease presents a challenge and, because of its low incidence, randomised controlled studies are impossible.

I am surprised by the high percentage of serious adverse effects of HBOT encountered in this study. The authors report that five out of 17 patients had serious adverse effects with two cases of pulmonary oedema, one hyperoxic seizure (which after careful reading turns out to be more likely a hypoglycaemic episode), one tympanic membrane perforation and one case of claustrophobia which occurred during the patient's first session. Even after discounting the case of claustrophobia, the remaining incidence of 24% is still extremely high compared to the expected incidence of side effects in this patient group. In the discussion (page 199, paragraph 2), it says "*complications such as oxygen toxic seizures and acute pulmonary oedema are directly related to high intra-arterial oxygen tensions and are well documented in the literature*". The quoted paper here (reference 14, Leach et al 1998) refers to pulmonary symptoms and subsequently pulmonary oxygen toxicity and not to acute pulmonary oedema.[2] Pulmonary oedema as a side effect purely of HBOT is extremely rare and we have not seen pulmonary oxygen toxicity in patients treated for 2 hours per day, as would be the case in MOE. Further on in the discussion (page 199, paragraph 2), the authors quote a recent review which has the wrong reference (this should be reference 21 not 18) and where they report a complication rate of 20%, whereas in the original quoted paper by Huang et al it is 1.83%.[3] Further on, the incidence of serious complications quoted in this publication by Saxby et al is 1.7% (they include pulmonary oedema, even though the original paper by Huang only talks about central nervous system toxicity), but the incidence in the original publication by Huang et al was 0.109%.[3]

At the 2010 Annual Scientific Meeting of the European Underwater and Baromedical Society, we presented a series of nine patients with MOE who received HBOT at Whipps Cross Hospital, London.[4] In our series, none of the patients experienced any severe adverse events during a similarly long treatment programme of 23 to 40 sessions. This treatment was sufficient to yield a benefit in seven of the nine patients (with benefit defined as both a significant improvement of symptoms – pain, discharge and cranial nerve palsies – and normalisation of inflammatory markers post-treatment).[4] We have similar positive results in the patient series in Plymouth (unpublished observations).

The high incidence of serious side effects reported by the authors gives me cause to wonder how patients in this retrospective study were screened for their suitability for HBOT. I am concerned that non-hyperbaric specialists reading this paper might conclude that the risk-benefit of using hyperbaric oxygen in MOE is in favour of avoiding its use, with a high risk (29%) of serious side effects and a very low benefit.

Indeed, we had problems convincing our local health authorities to fund treatment for our patients, hence a published paper talking about five out of 17 patients having serious side effects from the treatment would just reinforce their belief that HBOT is dangerous and not beneficial. Hyperbaric physicians should be careful when publishing data that could be interpreted in the wrong way by specialists unversed in hyperbaric medicine.

References

1 Saxby A, Barakate M, Kertesz T, James J, Bennett M. Malignant otitis externa: experience with hyperbaric oxygen therapy. *Diving Hyperb Med*. 2010;40:195-200.
2 Leach RM, Rees PJ, Wilmshurst P. Hyperbaric oxygen therapy. *BMJ*.1998; 317(7166):1140-3.
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4 Lechner M, Heywood R, Patel N, Ignatescu M. Hyperbaric oxygen therapy in malignant otitis externa. *Proceedings of the Annual Scientific Meeting of the European Underwater and Baromedical Society*; 2010. p. 52.

Mihaela Ignatescu
Consultant in Diving & Hyperbaric Medicine
Diving Diseases Research Centre
Plymouth, United Kingdom, PL6 8BU
E-mail: *< mihaela.ignatescu@ddrc.org>*

Reply

We thank Dr Ignatescu for her thoughtful comments on our recent case series of malignant otitis externa (MOE).[1] Dr. Ignatescu raises some interesting and important issues, and we are pleased with the opportunity to discuss these further. We agree the incidence of serious side effects is high in this patient group, but are perhaps less surprised that this is so than Dr Ignatescu. One of the reasons we wished to do this review of our experience was our clinical impression that these generally elderly patients with many co-morbidities were indeed prone to adverse effects of their therapies and of suffering poor outcomes despite all our efforts. Dr Ignatescu quotes our numbers correctly; five of 17 patients suffered significant adverse effects and this confirmed our clinical suspicion. Whether one interprets the seizure included here as hyperoxic or hypoglycaemic is of little consequence; this patient still suffered an adverse event of therapy. Please

note also that the relevant paragraph in our report starts "*Complications that might be attributed to HBO…*" That is, we accept there is some room to argue the true cause of some of these events.

We thank Dr Ignatescu for pointing out that the reference included concerning complications does not talk specifically about pulmonary oedema.[2] The intended additional reference specific to pulmonary oedema disappeared inadvertently in the drafting stage in our attempts to shorten this report so it was an acceptable length for publication. The intended reference was Weaver and Churchill 2001.[3] There are further references available in that article to support our statement that pulmonary oedema is a well-reported complication of HBOT. To quote from Weaver's introduction: "*Pulmonary edema is a rare complication of hyperbaric oxygen therapy. Abel et al estimate the incidence of pulmonary edema associated with hyperbaric oxygen therapy at 1 in 1,000, and Riddick suggested that patients with reduced cardiac ejection fractions (EFs <40%) should not receive hyperbaric oxygen therapy because of the risk of acute pulmonary edema*". We absolutely agree that pulmonary oxygen toxicity is not a problem in patients receiving daily HBOT at the pressures used for these patients, nor did we suggest that to be the case.

Dr Ignatescu is also correct that the reference '18' in the discussion (page 199) should have been '21' and we apologise for any confusion. There should have been no reference given after the first of these two sentences. We believe, however, that Dr Ignatescu has misinterpreted the complication rates given in Huang 2006[4] as a result of mixing up quoted incidences *per treatment* and *per patient*. We agree with the figures quoted by Dr Ignatescu, but note that those we quoted are per patient, not per treatment. This is clearly given in Table 2 in Huang (48/240 or 20%) and we believe this figure is more easily interpreted by a non-expert. We had felt this was understood from the few lines above where we were talking about the proportion of patients suffering adverse events, but concede that it may have been better to emphasise this again in this passage so the reader could not possibly be confused by the two different ways of looking at the rate of complication.

We congratulate Dr Ignatescu on the success of HBOT in her group of patients at Whipps Cross Hospital and urge her to publish this is in a listed journal to add to the discoverable literature on this subject. We think the most important statement in this regard in her letter is: "*The high incidence of serious side effects reported by the authors gives me cause to wonder how patients in this retrospective study were screened for their suitability for HBOT.*" We agree – the difference in outcome probably arises from differences in our clinical decision making. We also agree with the implication that your group denied HBOT to some of the patients whom we would have accepted. Adopting a more conservative policy is indeed likely to identify those more able to tolerate HBOT; thus the Whipps Cross series has a good outcome with a low complication rate. We would argue that you may have refused patients who could have benefitted, and that our broader inclusion criteria demonstrates that only two of 17 (11.8%) could not ultimately tolerate the course of HBOT offered. Among those who did get HBOT, we perhaps contributed to improved outcomes that would not have occurred if HBOT had been withheld on safety grounds. Which of these interpretations is correct is, of course, unknowable without good comparative trials that we both agree are not possible. We simply do not know which strategy will produce the greatest net benefit.

It is possible, as Dr Ignatescu suggests, that non-hyperbaric physicians reading our study might conclude that HBOT is of little benefit in MOE. We are not clear this means we should avoid reporting our experience as is implied in the letter. We do not think it is appropriate to report our patients in the best possible light for the application of HBOT, but rather that we are honest about our experience. We have no doubt both our groups have been so, and the difference in our reported experiences contains a lot of subtle and unknown biases that have affected our outcomes. It is the primary care team physicians who must decide how they will interpret such evidence – hopefully with the guidance of specialist hyperbaric physicians who understand their literature and have appropriate experience. In this, there is no substitute for having people in our field who think deeply about what they do. We congratulate the group at Whipps Cross for being in that category.

References

1 Saxby A, Barakate M, Kertesz T, James J, Bennett M. Malignant otitis externa: experience with hyperbaric oxygen therapy. *Diving Hyperb Med*. 2010;40:195-200.

2 Leach RM, Rees PJ, Wilmshurst P. Hyperbaric oxygen therapy. *BMJ*. 1998;317(7166):1140-3.

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Michael Bennett, Consultant, Department of Diving and Hyperbaric Medicine.
Alex Saxby, Visiting Medical Officer, Department of Otorhinolaryngology.
Joanne James, Nursing Unit Manager, Department of Diving and Hyperbaric Medicine.
The Prince of Wales Hospital, Randwick, Australia
E-mail: *<m.bennett@unsw.edu.au>*

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