Letter to the Editor

Dear Editors,

We have read the recent article of Orsted et al. (1) with a lot of interest and we acknowledge and congratulate them for their efforts in trying to better define the level of evidence on topical pressurised oxygen therapy (TPOT) for wound healing in their paper entitled 'Evidence-based practice standards for the uses of topical pressurised oxygen therapy’. However, some statements, used as premises in their article, are confusing and some others might lead the reader to some incorrect interpretations on the effects and complications of systemic hyperbaric oxygen therapy (sHBOT) especially in the context that TPOT could be perceived as an option to sHBOT. We believe that the expertise of our group in the field of sHBOT in the last 10 years puts us in a good position to discuss beneficial effects and risks of sHBOT as we have treated more than 1200 patients combining more than 15000 sHBOT sessions in a period of 9 years in a Perry Duoplace hyperbaric chamber (R. Belley, unpublished presentation)

Orsted et al. state that:

...Systemic hyperbaric oxygen therapy is a treatment modality in which a patient breathes 100% oxygen at a pressure greater than one atmosphere: the pressure of air at sea level... (Orsted et al., 2012)

...Topical pressurised oxygen therapy is also considered hyperbaric in that it also delivers 100% oxygen at pressure greater than one atmosphere... (Orsted et al., 2012)

The definition of sHBOT given by Orsted et al. is consistent with the definition by the (UHMS) (2). However, stating that TPOT is considered as hyperbaric is clearly inconsistent with UHMS’s past statements on the subject:

...Topical oxygen should not be termed hyperbaric oxygen since doing so either intentionally or unintentionally suggests that topical oxygen treatment is equivalent or even identical to hyperbaric oxygen... (3)

TPOT delivers 100% oxygen at a pressure of barely 1·03 atmosphere absolute (ATA), which would not be considered hyperbaric oxygen.

Orsted et al. state:

...there is risk of complications such as seizures, damage to the tympanic membrane of the ear (barotraumas), and damage to the retinal nerves (retinopathy)... (Orsted et al. 2011)

Any treatment option has its share of complications. Seizures in a hyperbaric environment are related to oxygen toxicity. The risk of seizures in hyperbaric environment is minimal and strongly related to depth of pressurisation. The literature report a 0·01–0·03% (1–3 in 10 000) incidence rate at pressures between 2 and 3 ATA, and a 0·6 (6 in 1000) incidence rate at pressures between 2·6 and 3·0 ATA (4). Most sHBOT protocols for wound healing use a 2·0–2·5 ATA pressure depth (5), thus minimising the risk of seizure.

Barotraumas are by far the most important complication of sHBOT in our hyperbaric unit. Côté in 2009 (M Côté, unpublished results) found a 26% incidence of barotraumas in patients treated for various indications with sHBOT, only 8% needing a myringotomy. These results are consistent with what is reported in the literature, with incidence rates between 2% and 45% (6,7)

Orsted et al. write that retinal nerve damage is a complication of sHBOT. This is a complication we have never encountered in our hyperbaric unit. The literature is also very thin on that matter. The risk of retinal damage is practically an inexistent under exception under extreme conditions of hyperbaric exposure (8) (very high pressurisation, not done for wound healing protocols), a premature retina (such as in newborns) (9) and a history of retro bulbar neuritis (10).

Orsted and Poulson state:

...if patients have diabetes their glucose levels could also be affected by an increased pO2... (Orsted et al., 2011)

Glucose levels in diabetic patients can in fact be affected by acute pressurisation and hyperoxia (11). sHBOT affects insulin secretion by a mechanism not yet fully understood. Our clinical experience shows that slight to moderate hypoglycaemia is common during pressurisation in diabetic patients, although trivial and without any consequences. To prevent severe hypoglycaemia, glycaemic control protocols at the beginning of every sHBOT session are used in most hyperbaric units treating diabetic patients. Long-term glycaemic control has also been evaluated and it is suggested that long-term glycaemic control could be improved with sHBOT (12).

Our research group is currently recruiting patients treated with sHBOT for a study (13) that will take a closer look at cardiometabolic parameters, including glycaemic control.

Although sHBOT has potential minimal side effects, it has been shown by high level studies to be successful in treating wounds, especially diabetic foot wounds (14,15). The International Working Group on the Diabetic Foot, through a systematic review concluded recently, show that only sHBOT and possibly negative pressure wound therapy are justified as newer therapies to enhance the healing of chronic ulcers of the foot in diabetic patients (16). This is not the case with TPOT, as evidenced by Orsted et al. in their article.
Orsted et al. state:

...Topical pressurised oxygen therapy is not dependant on systemic circulation reaching the wound bed... (Orsted et al., 2011)

sHBOT is also effective if systemic circulation is inadequate, such as wounds associated with peripheral arterial disease (PAD) of the lower limb. In fact, partial pressure of oxygen of an hypoxic wound can increase from 10 mmHg at air at 1 ATA to 400 mmHg at 100% oxygen at 2.4 ATA (17). Transcutaneous oximetry monitoring is a modality used in our hyperbaric unit for every patient with an ischaemic wound of the lower limb and we clearly demonstrate on a day to day basis that normobaric and hyperbaric hyperoxia will increase the partial pressure of oxygen around a wound afflicted with poor arterial circulation, such as PAD of the lower limb. sHBOT increases partial pressure of oxygen in the entire body including ischaemic wounds and it is important to understand that the benefits are related not only to local hyperoxia but more importantly to the systemic oxidative stress. It has been shown that sHBOT increases Reactive Nitrogen Species and Reactive Oxygen Species causing wound neo-vascularisation, healing and improved post ischaemic tissue survival (18). From a clinical point of view, our data suggest that cardiometabolic parameters are modified with consecutive sessions of sHBOT (19) which support the known hypothesis that the effect of sHBOT involves more than a topical effect on the wound.

In conclusion, we hope that some elements on sHBOT as discussed in the Orsted et al. article have been clarified and put in perspective in order to better capture the essence of the main topic, which is the use of topical pressurised oxygen therapy.

References


Reply:

Response to Dr Richard Belley MD, CCFP, BSc; Dr Dominique Buteau MD, CCFP(EM); Dr Marie-Ludivine Chateau-Degat PhD

One of the purposes of a paper that explores new therapies is to generate discussion to support the best possible use of...
the therapy, and we are pleased doctors Belley, Buteau and Chateau-Degat have provided their comments.

We recognised that new therapies can be confusing to health-care professions, so as a team consisting of both wound care leaders and/or users of topical pressurised oxygen therapy we worked together with the supporting evidence used by the manufacturers and distributors to help clarify where topical pressurised oxygen therapy fits it as a wound healing modality.

The following responses to clarify our original statements are supported by the evidence indicated in our paper. We welcome additional discussion as we move forward to further improve understanding of this new technology.

**Statement number 1:** The definition of hyperbaric is stated as any pressure above normobaric or 760 mmhg. Since topical pressurised oxygen therapy rises to 798 mmhg it is, by definition, hyperbaric. This is also demonstrated by the general gas laws and by Boyles law.

**Statement number 2:** There were no statements intentionally or unintentionally made that topical pressurised oxygen therapy is identical or equivalent to systemic hyperbaric oxygen therapy (sHBOT). Topical pressurised oxygen therapy is hyperbaric but has a different route of administration – which is clearly identified in our paper.

**Statement number 3:** Complications of sHBOT are identified by Undersea and Hyperbaric Medical Society (UHMS). And though they might be few in number in terms of incidence they are still listed by UHMS as caveats to the therapy and we believed it was important to mention them to give a fuller picture of the therapy.

For example, wound healing does occur above 2.4 atmospheres absolute (ATA) in instances of treating necrotising fasciitis, which is at 3.0 ATA, but air breaks must be given to help curb seizure; by UHMS standards and protocols these caveats do exist.

**Statement 4:** Hypoglycemia is a listed concern with sHBOT. Protocols indicate that all persons with diabetes are tested prior to entrance to the chamber. If the glucose levels are normal or somewhat below, juice is usually provided to the patient to curb a hypoglycemic event during the dive. Diabetic foot ulcers have been shown to improve in the study by Blackman and Aburto.

**Statement 5:** All patients to receive HBOT must receive an oxygen challenge utilizing transcutaneous oxygen (TCOM). If the peripheral arterial disease (PAD) is severe, the partial pressure of oxygen (pO2) will not rise via TCOM monitoring. If the oxygen challenge is negative, the PAD must be dealt with via revascularization or the treatment is not an option. Topical pressurised oxygen therapy despite PAD can assist with neovascularization and the reactive oxygen species (ROS) because it is topical and not dependent on arterial circulation.

By examining the most recent evidence and collaborating with industry we have achieved a framework by which clinicians and end users can appropriately evaluate the promotional and evidential material used to support their decision making around new wound technologies.

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