

SUMMARY

INDICATIONS FOR HYPERBARIC OXYGEN THERAPY: UPDATE

Introduction

During the first half of the 20th century, hyperbaric oxygen (HBO) therapy was used to treat decompression sickness. Other indications have been added over the years, with the result that the Hyperbaric Oxygen Therapy Committee of the Undersea and Hyperbaric Medical Society (UHMS) now recommends HBO therapy for the prevention or treatment of the following 13 conditions: 1) decompression sickness; 2) gas embolism; 3) carbon monoxide poisoning; 4) radionecrosis; 5) problem wounds; 6) thermal burns; 7) skin and tissue graft problems; 8) gas gangrene; 9) necrotizing soft-tissue infections; 10) refractory osteomyelitis; 11) intracranial abscess; 12) crush injuries, compartment syndromes and acute traumatic ischemia; and 13); exceptional blood loss anemias. However, with the exception of emergency situations such as decompression sickness and gas embolism, the applications of HBO therapy are still debated in the scientific literature.

In this context, the Minister of Health and Social Services asked the Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) to review the current state of knowledge concerning the use of HBO therapy to prevent and treat these 13 conditions. More specifically, it would like to know if, since the publication of the report by the Conseil d'évaluation des technologies de la santé (CETS, AETMIS's predecessor) in 2000, new research has yielded any evidence regarding the efficacy of this technology and if other indications could be added to these 13. It will be noted that AETMIS recently produced two reports on the role of HBO therapy in managing cerebral palsy and autism, two indications that are not recognized by the learned societies.

Results

The quantitative and qualitative studies published since 2000 on the 13 indications and a few other conditions treated with HBO therapy were analyzed.

1. Decompression sickness

The UHMS and the European Committee for Hyperbaric Medicine (ECHM) recommend the treatment of decompression sickness with HBO therapy on the basis of data from basic physics, of observational studies and of clinical experience. This is because it is difficult to conduct randomized controlled trials (RCTs) on this indication, and in this case, one or two sessions of HBO therapy are sufficient to save a patient's life. A systematic Cochrane review (2007) including two RCTs shows that fewer sessions of HBO therapy are required if the patient is administered a nonsteroidal antiinflammatory (NSAID) or if a mixture of helium and oxygen is used in the hyperbaric chamber.

2. Gas embolism

The UHMS and the ECHM recommend HBO therapy for the treatment of gas embolism, based, once again, on data from basic physics, on observational studies and on clinical experience. Conducting RCTs is difficult in such cases, which require emergency treatment.

3. Carbon monoxide poisoning

One RCT and three systematic literature reviews have compared the efficacy of normobaric and hyperbaric oxygen therapy in reducing the neurological sequelae of carbon monoxide poisoning. The RCT identified is one of the most important ones on reducing late or permanent neurological sequelae, but its results have sparked

a debate. Furthermore, the meta-analysis presented in one of the three systematic reviews does not, because of the heterogeneity of the studies, which used different HBO protocols and different criteria, permit the conclusion that HBO therapy is effective in eliminating late or permanent neurological sequelae. Additional high-quality studies would help to definitively conclude that HBO therapy is effective in treating the short- and long-term effects of this type of poisoning.

The UHMS and the ECHM recommend that HBO therapy be used to treat patients with carbon monoxide poisoning who are at high risk for complications, i.e., patients who lose consciousness for a brief or prolonged period of time, those who present with respiratory, cardiac or neurological signs and symptoms, and pregnant women.

4. Radionecrosis

Four RCTs, two assessment reports and four systematic literature reviews aimed at evaluating the efficacy of HBO therapy in preventing and treating radionecrosis were identified. The new data from the recent primary studies do not provide a clear answer as to the efficacy of HBO therapy in treating radionecrosis, except the study concerning radiation proctitis, where significant symptomatic relief was observed after three months. The efficacy of HBO therapy in preventing radionecrosis of the brain after stereotaxic surgery for metastases still needs to be confirmed by new studies. A systematic Cochrane review (2005) presents the results of six RCTs individually, since it was impossible, given the heterogeneity of the studies, to perform a meta-analysis. This review shows a significant improvement in the condition of patients treated with HBO therapy for: 1) mandibular osteoradionecrosis prophylaxis and alveolar healing after tooth extraction in an irradiated area; 2) improving the healing of wounds due to the reconstruction of an irradiated mandible; 3) the healing of soft tissues and musculocutaneous grafts after major surgery in an irradiated area; and 4) the treatment of hemorrhagic radiation proctitis. However, this review does not present any robust scientific data establishing that HBO therapy has a clinical effect on central or peripheral nerve tissue. Lastly, the UHMS and the ECHM recommend that HBO therapy be used as a treatment for hemorrhagic radiation cystitis.

5. Problem wounds: diabetic lesions and venous ulcers

There are four RCTs and five systematic literature reviews on the treatment of diabetic lesions with HBO therapy. The data from the primary studies indicate an improvement in the healing rate and a decrease in the risk of major amputation. However, since these studies have methodological weaknesses, the authors recommend that better-quality trials be conducted to confirm the effect of HBO therapy on diabetic wounds. A systematic Cochrane review (2004) including five RCTs evaluated the effect of adjuvant HBO therapy on the healing of four types of chronic wounds (diabetic foot ulcer, venous leg ulcer, arterial leg ulcer and decubitus ulcer) and on the risk of amputation. There was no significant difference in the diabetic ulcer healing rate at six weeks or six months, but a significant improvement was observed at 12 months in the patients who underwent HBO therapy. The risk of major amputation due to a diabetic ulcer was significantly reduced (by 25%) with HBO therapy. These findings are from the above-mentioned primary studies, which also have methodological weaknesses.

Nonetheless, these results suggest that HBO therapy combined with conventional therapy is effective in treating delayed healing (diabetic foot, venous ulcers) within the framework of multidisciplinary management. On the other hand, there are still no robust scientific data establishing that HBO therapy has a clinical effect on arterial leg ulcers, decubitus ulcers or vasculitis.

6. Problem wounds: severe burns

Since 2000, there have been no RCTs on the use of HBO therapy to treat severe burns. A systematic Cochrane review published in 2004 concluded that there was not enough evidence to determine whether or not HBO therapy is effective in treating thermal burns. Based on expert consensus, the UHMS and the ECHM still recommend HBO therapy for treating second-degree thermal burns that cover more than 20% of the body.

7. Problem wounds: skin and tissue grafts

Given the lack of new data, there is still insufficient evidence on the efficacy of HBO therapy in enhancing skin graft and musculocutaneous flap survival, except in irradiated areas (as mentioned in the section on radionecrosis). It will be necessary to conduct clinical trials on this matter and compare HBO therapy used alone or in combination with other surgical and pharmacological measures that also improve angiogenesis and granulation tissue formation. Based on the expert consensus, the UHMS and the ECHM recommend HBO therapy for improving the healing of compromised grafts, especially in the presence of tissue ischemia or in irradiated areas.

8. Infectious diseases: gas gangrene

Since 2000, one case series study and one systematic literature review of poor methodological quality have been added to a few narrative reviews concerning gas gangrene. Because of the noncomparative nature of case series studies, it is difficult to evaluate the therapeutic effect of HBO therapy, which, according to the authors, is positive. HBO therapy is also recommended, by expert consensus, as an adjuvant to antibiotic therapy and surgery in patients at high risk for morbidity and death or who are immunodeficient, but this recommendation is not supported by new evidence. It is difficult to conduct randomized controlled trials on this rare and often fatal infection, which requires emergency treatment.

9. Infectious diseases: necrotizing soft-tissue infections

One case series study, one systematic literature review of poor methodological quality and a few narrative reviews report the beneficial effects of HBO therapy for treating necrotizing soft-tissue infections. These findings will need to be confirmed by controlled studies. HBO therapy is therefore still recommended, by expert consensus, as an adjuvant to antibiotic therapy and surgery in patients at high risk for morbidity and death or who are immunodeficient, but this recommendation is not supported by new evidence.

10. Infectious diseases: refractory osteomyelitis

Since 2000, a few case series studies, one systematic literature review of poor methodological quality, and a few narrative reviews on osteomyelitis have yielded results that vary according to the location of the affected tissues. HBO therapy is recommended, by expert consensus, for the treatment of osteomyelitis because of its recurrence and complications. Without the support of new data, this treatment modality is an adjuvant to nutritional therapy, surgery and antibiotic therapy for treating stages IIIB and IVB (Cierny-Mader classification) refractory osteomyelitis within the framework of a multidisciplinary treatment protocol.

11. Infectious diseases: intracranial abscess

The favourable results with HBO therapy reported in a few case series studies and narrative reviews of the literature on intracranial abscesses still need to be confirmed by controlled trials. HBO therapy is recommended, by expert consensus, for treating deep or multiple intracranial abscesses, especially in immunodeficient patients, patients with high surgical risk and those who do not respond to conventional treatment.

12. Crush injuries, compartment syndromes and acute traumatic ischemia

Since 2000, a few case series studies, three systematic literature reviews and a few narrative reviews have shown favourable results for the treatment of crush injuries, compartment syndromes and acute traumatic ischemia. According to the experts, HBO therapy is an adjuvant to the conventional therapeutic modalities for acute peripheral traumatic ischemia or crush injuries (Gustilo type IIIB and C open fractures) if there is a risk of functional loss or the loss of a limb or if the patient's life is in jeopardy.

13. Specific anemias

One systematic literature review and a few narrative reviews have examined specific anemias but have not raised the level of evidence. HBO therapy is recommended, by expert consensus, for the treatment of exceptional blood loss when blood

transfusion is not an option. However, additional clinical studies will need to be carried out to define the role of HBO and compare its efficacy with that of the other medical options available for treating this problem.

14. Other indications

A number of studies have examined other potential applications of HBO therapy. Although they have shown encouraging or promising results, it must be concluded that the efficacy evidence for HBO therapy is still insufficient and that new studies are needed to justify its clinical use. The potential applications examined in this report are as follows:

- malignant conditions: tumour sensitisation to radiotherapy;
- sports injuries: healing and pain relief;
- acute coronary syndrome: adjuvant therapy;
- cardiopulmonary surgery: prevention of inflammatory and neurological effects;
- migraines and episodic or chronic headaches: relief and pain reduction;
- Bell's palsy: healing;
- stroke and head injury: decrease in mortality and improved functional status;
- multiple sclerosis: symptomatic relief;
- poisoning due to different substances (quinine, cyanide, opium): attenuation of neurological sequelae.

With regard to the treatment of idiopathic sudden sensorineural hearing loss, the current knowledge indicates that HBO therapy would significantly reduce hearing loss during the first few weeks following its occurrence. However, the clinical importance of this gain is uncertain and cannot, therefore, justify, at this time, the systematic use of HBO therapy without the support of new studies. However, the ECHM's experts maintain the 1994 recommendation, which advises the use of HBO therapy to treat this condition, until an ongoing European study on this matter is completed.

Lastly, the role of HBO therapy in managing cerebral palsy and autism is exhaustively examined in two recent AETMIS reports (2007). Based on the current state of knowledge, these applications are

still experimental, and rigorous controlled clinical trials are needed to demonstrate their efficacy.

Conclusion

The main objective of this report was to update the previous report (published by CETS in 2000) on the recognized indications for hyperbaric oxygen (HBO) therapy. Given the paucity of new studies and the fact that a number of them are of poor quality, AETMIS has, to a large extent, based its assessment on expert consensus, the two main ones being from the Hyperbaric Oxygen Therapy Committee of the Undersea and Hyperbaric Medical Society (UHMS) and the European Committee for Hyperbaric Medicine (ECHM).

At the end of its assessment, AETMIS concludes that, on the whole, the recommended indications for hyperbaric oxygen therapy remain the same, although there is now additional information. Based on the evidence (classified into three levels: A - high; B - medium; C - low), the list of indications is now as follows:

I. Recommended indication for prevention:

- Osteoradionecrosis after tooth extraction in an irradiated area (level of evidence: B; no new data).

II. Recommended indications as first-line therapy:

- Decompression sickness (level of evidence: C).
- Complicated venous or arterial gas embolism (level of evidence: C; no new data).

III. Recommended indications as second- or third-line therapy:

- Carbon monoxide poisoning (level of evidence: B).
- Gas gangrene (level of evidence: C; no new data).
- Infectious necroses other than gas gangrene (level of evidence: C; no new data).
- Mandibular osteoradionecrosis, radionecrosis of soft tissues and musculocutaneous grafts after major surgery in an irradiated area, hemorrhagic radiation proctitis (level of evidence: B) and hemorrhagic radiation cystitis (level of evidence: C; no new data).

- Problem wounds (diabetic lesions, venous leg ulcers) (level of evidence: B).
- Skin and musculocutaneous grafts in ischemic areas (level of evidence: B; no new data).
- Refractory osteomyelitis (level of evidence: C).
- Intracranial abscess (level of evidence: C).
- Ischemic and traumatic lesions: crush injuries, compartment syndromes and other acute traumatic ischemia (level of evidence: B; no new data).

IV. Recommended indications as optional therapy:

- Thermal burns (level of evidence: C; no new data).
- Specific anemias (level of evidence: C; no new data).

For most of these indications, the parameters for administering HBO therapy (optimum duration of exposure, pressure, frequency of sessions) have yet to be determined.

Lastly, according to the ECHM, HBO therapy can be an optional treatment modality for idiopathic sudden sensorineural hearing loss during the first few weeks following its occurrence (level of evidence: B). However, according to this assessment report, new studies are required in order to justify the systematic use of HBO therapy for this particular type of hearing loss, since the clinical importance of the benefits that it confers is uncertain.

For other conditions, it cannot be established from the available evidence that HBO therapy is effective. They are malignant conditions, sports injuries, acute coronary syndrome, cardiopulmonary surgery, migraine, Bell's palsy, head injury, stroke and multiple sclerosis. However, the ECHM expert consensus states that HBO therapy may be an optional treatment for stage IV neuroblastoma, pneumatosis cystoides intestinalis, and acute ischemic ophthalmological disorders. Lastly, in two recent reports (2007), AETMIS concludes that HBO therapy is an experimental treatment for cerebral palsy and autism, two indications that are also not recognized by the learned societies.

It should be noted that few indications for hyperbaric oxygen therapy have been rigorously studied and that the evidence is scarce. Obviously, for ethical reasons, certain conditions are not easily amenable to scientific research. Although they are not entirely concordant, the expert consensus are thus the main foundation for supporting and justifying the use of HBO therapy for most of the clinical indications. These expert consensus are also opening up interesting avenues for new studies of better methodological quality and future clinical experiments.