Hyperbaric oxygen therapy for brain injury, cerebral palsy, and stroke

CRD summary
This review aimed to assess the benefits and harms of hyperbaric oxygen therapy (HBOT) for brain injury, cerebral palsy and stroke. The authors concluded that there was inadequate evidence on the benefits and harms of HBOT for brain injury, cerebral palsy and stroke. This was a well-conducted review and the authors' conclusions are appropriate given the conflicting evidence reviewed.

Authors' objectives
To assess the benefits and harms of hyperbaric oxygen therapy (HBOT) for brain injury, cerebral palsy and stroke.

Searching
MEDLINE, Pre-MEDLINE, EMBASE, CINAHL, The Cochrane Library, Health Technology Assessment Database, HealthSTAR, AltHealthWatch and MANTIS were searched from inception to March 2001; search terms were reported. The authors updated their searches of MEDLINE, PreMEDLINE, EMBASE and CINAHL in July 2003. The authors also searched the database of the Undersea and Hyperbaric Medical Society, Database of Randomised Controlled Trials in Hyperbaric Medicine, proceedings of the International Congress on Hyperbaric Medicine conferences and the database of National Baromedical Services, Inc. The authors intended to search the database of the European Underwater and Baromedical Society, but they did not receive a response to their requests for access to the database. The authors handsearched the reference lists of all included studies and the references from the Textbook of Hyperbaric Medicine. Experts involved in the review provided articles and meeting abstracts from their personal collections. Only studies published in English were eligible for inclusion in the review.

Study selection
Studies of hyperbaric oxygen therapy (defined as any treatment using 100% oxygen supplied inside a hyperbaric chamber pressurised to greater than one atmosphere) in patients with brain injury from any cause, cerebral palsy of any aetiology or thrombotic stroke were eligible for inclusion. Studies of patients with progressive neurological diseases, acute infectious processes, radiation sensitisation of brain tumours and reports of treating eye damage or sudden deafness were excluded. Studies of hyperbaric oxygen therapy for approved indications such as acute carbon monoxide poisoning or acute air embolism were also excluded. All study designs except for case reports and small case series were eligible for inclusion. Uncontrolled before and after studies and time series studies were eligible for inclusion if they included at least five participants and outcome measures were reported before and after hyperbaric oxygen therapy. Studies that reported any clinical endpoint were eligible for inclusion. The authors stated that they focused on health outcomes that a patient would experience, rather than intermediate outcomes.

Studies of head injury patients included adults and children. Severity included those in a coma. Studies of cerebral palsy patients were all in children. Studies of stroke patients included those who had suffered a stroke recently to those no longer undergoing therapy who had suffered a stroke up to 172 months earlier. Outcomes measured included mortality rate, coma/consciousness, intracranial pressure, neurological assessments, functional assessments, neurodevelopmental assessments, communication assessments, disability scales and adverse events. Further details of all included studies were presented in the report.

Two reviewers independently assessed studies for inclusion in the review; disagreements were resolved through consensus.

Assessment of study quality
For controlled trials the following quality items were assessed: randomisation/allocation concealment; comparability of groups at baseline; timing of baseline measures; intervention; outcome measures; timing of follow-up measurements; loss to follow-up; handling of dropouts or missing data; masking; statistical analysis; and other general concerns.

For observational studies the following quality items were assessed: exposure measurement; other interventions;
comparability of groups at baseline or establishment of a stable baseline; consideration of potential confounders; timing of follow-up measurements; outcome measures used; and other general concerns.

Each study was assigned an overall rating of good, fair or poor, according to the US Preventive Services Task Force method (further details were given in the report).

External validity was also assessed (whether the study population was representative of the underlying patient population).

The authors did not state how the validity assessment was performed.

**Data extraction**
Data were extracted by one reviewer and checked by a second reviewer; disagreements were resolved through consensus.

**Methods of synthesis**
A narrative synthesis of the controlled trials and observational studies was presented.

**Results of the review**
Seventy-one studies were included in the review, including 10 controlled trials, 29 observational studies and 32 studies that were published as abstracts.

**Brain injury (three randomised controlled trials and nine observational studies):** Evidence was conflicting. One fair-quality randomised controlled trial found reduced mortality after one year of follow up in patients who received hyperbaric oxygen therapy, but another fair-quality randomised controlled trial found no difference in mortality rates after one year of follow-up. One of these trials also found that survivors in the hyperbaric oxygen therapy group were more likely to be severely or completely disabled than survivors in the control group. The other randomised controlled trial was poor quality.

**Cerebral palsy (two randomised controlled trials and three observational studies):** The two randomised controlled trials (one fair quality and one uncertain quality) reported no difference in improvements for those patients who received hyperbaric oxygen therapy and those who did not. In one study, patients in the control group received pressurised room air. Conversely, observational studies (one fair quality and two poor quality) reported improvements on subjective measures and motor function for patients who received hyperbaric oxygen therapy.

**Stroke (four randomised controlled trials, one non-randomised controlled trial and 17 observational studies):** Evidence was conflicting. Three fair-quality randomised controlled trials found no benefit in terms of neurological outcomes for patients who received hyperbaric oxygen therapy over those who received pressurised room air or low-pressure oxygen. Two poor-quality controlled trials found improved neurological outcomes on some measures for patients who received hyperbaric oxygen therapy. Most observational studies reported improved results for patients who received hyperbaric oxygen therapy.

**Authors' conclusions**
There was inadequate evidence on the benefits and harms of hyperbaric oxygen therapy for brain injury, cerebral palsy and stroke. Further research was required.

**CRD commentary**
The review addressed a clear question and was supported by appropriate inclusion criteria. The search strategy was extensive and included sources of unpublished data, but only studies reported in English were eligible for inclusion, which increased the potential for language bias. Study selection and data extraction were done in duplicate, which reduced the potential for reviewer error or bias. Study validity was assessed using appropriate criteria and the results of the validity assessment were presented in the evidence tables and discussed in the review synthesis. Comprehensive details of all the included studies were provided. Given the differences in study design and patient characteristics, a narrative synthesis appeared appropriate. This was a well-conducted review and the authors' conclusions are appropriate.
given the conflicting evidence reviewed.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that future research of hyperbaric oxygen therapy should include dose-ranging and safety studies to establish the optimum course of hyperbaric oxygen therapy to evaluate in future outcome studies. Several treatment options should be assessed in future studies. Outcomes should include caregiver burden and patients’ functional outcomes. The authors identified several barriers to conducting controlled trials of hyperbaric oxygen therapy and discussed different strategies to attempt to overcome these barriers.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.