

To Dive or Not to Dive? Use of Hyperbaric Oxygen Therapy to Prevent Neurologic Sequelae in Patients Acutely Poisoned with Carbon Monoxide

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SYSTEMATIC REVIEW SOURCE

This is a systematic review abstract, a regular feature of the *Annals'* Evidence-Based Emergency Medicine (EBEM) series. Each features an abstract of a systematic review from the *Cochrane Database of Systematic Reviews* and a commentary by an emergency physician knowledgeable in the subject area.

The source for this systematic review abstract is: Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning (Cochrane Review). In: *The Cochrane Library*, Issue 2. Chichester, UK: John Wiley & Sons, Ltd; 2004.

OBJECTIVE

To assess the effectiveness of hyperbaric oxygen therapy compared to normobaric oxygen therapy for the prevention of neurologic sequelae in patients acutely poisoned with carbon monoxide.

DATA SOURCES

A comprehensive search of MEDLINE (1966 to October 2004), EMBASE (January 1980 to September 2004), and the Controlled Trials Register of the Cochrane Collaboration was conducted. The reviewers also manually reviewed bibliographies of identified articles, and additional references were sought from recognized content experts. The review is considered up to date as of November 2004.

STUDY SELECTION

Randomized controlled trials involving nonpregnant, adult patients acutely poisoned with carbon monoxide, regardless of severity, with sufficient or unclear allocation concealment.

DATA EXTRACTION AND ANALYSIS

Two reviewers independently extracted data from each trial about the number of randomized patients, types of participants, the dose and length of the treatment, and the prevalence of neurologic symptoms at follow-up.

MAIN RESULTS

Six randomized controlled trials were included in this review; 2 of the 6 trials represented incomplete publications (1 abstract, 1 interim analysis). Four of the 6 trials found no benefit of hyperbaric oxygen therapy for the reduction of adverse neurologic outcomes, whereas 2 others did. In a pooled analysis, no statistically significant decrease in neurologic sequelae was associated with hyperbaric oxygen therapy (odds ratio 0.78; 95% confidence interval 0.54 to 1.12). However, because of significant methodologic and statistical heterogeneity among the trials, this result should be interpreted with caution. Furthermore, analysis or design flaws were present in all trials.

CONCLUSIONS

Previously published randomized trials do not establish whether the use of hyperbaric oxygen therapy in patients with acute carbon monoxide poisoning reduces the incidence of adverse neurologic sequelae.

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COMMENTARY: CLINICAL IMPLICATION

Carbon monoxide is a notorious silent killer and accounts for more deaths annually in the United States than any other poison.¹ More than 16,000 exposures to carbon monoxide were reported to the American Association of Poison Control Centers in 2003; however, the actual number of exposures in the United States each year is probably much greater because many cases go undetected or unreported.² Individuals who survive poisoning with carbon monoxide are at risk for developing adverse neurologic sequelae. Treatment options consist of supportive measures combined with normobaric oxygen therapy or hyperbaric oxygen therapy. Some authors^{3,4}

have recommended the use of hyperbaric oxygen therapy to prevent the adverse neurologic sequelae that can develop in patients several weeks after an acute exposure to carbon monoxide.

This Cochrane Review identified all published randomized controlled trials of hyperbaric oxygen therapy versus normobaric oxygen therapy for the treatment of acute carbon monoxide poisoning. Overall, the authors conclude from the evidence accumulated from 6 trials involving 1,335 patients that there is insufficient evidence to conclude that hyperbaric oxygen prevents late neurological sequelae. The authors, however, warn readers to cautiously interpret the results because of heterogeneity, methodological weaknesses, and statistical flaws. For example, only 2 trials^{4,5} received the highest scores based on methodologic quality rating (5/5 Jadad scale),⁶ and they are the only trials to date in which control patients received sham treatment in a hyperbaric chamber; however, the results of these 2 studies should still be interpreted judiciously because both have analysis and design flaws.

Patients in both arms of the study by Scheinkestel et al⁵ were treated with continuous normobaric oxygen for 3 days, which is not typical practice. Although this treatment could potentially bias the results toward the null if the longer duration of therapy actually decreased the control event rate, the control event rate in this study was actually high (0.62) compared with the overall combined control event rate of all trials included in this review (0.34). The high control event rate can be explained by the large proportion of patients enrolled with severe poisoning (73%). The most significant limitation of the Scheinkestel et al⁵ trial was the significant number of subjects lost to follow-up; less than 50% of randomized subjects were available for outcome assessment at 4 to 6 weeks.

The study by Weaver and colleagues⁴ demonstrated a favorable effect for patients with moderate to severe poisoning treated with hyperbaric oxygen therapy; however, the interpretation of the results is clouded by the following issues: (1) patients treated with normobaric oxygen tended to be sicker (ie, longer mean exposure to carbon monoxide and greater prevalence of cerebellar dysfunction at baseline) than those treated with hyperbaric oxygen; and (2) the original endpoint of the study⁷ was delayed neurologic sequelae, whereas the final publication describes the endpoint as all neurologic sequelae (ie, persistent neurologic sequelae and delayed neurologic sequelae).

The question then remains: to dive or not to dive? Based on the results of this Cochrane Review, hyperbaric oxygen therapy should not be used routinely in patients with acute carbon monoxide poisoning. Some patients, in particular those with moderate to severe poisoning, may benefit from treatment with hyperbaric oxygen.

TAKE HOME MESSAGE

It remains unclear which patients with carbon monoxide poisoning will not require treatment with hyperbaric oxygen

therapy. Further research is needed to define which patient subgroup, if any, will benefit from the use of hyperbaric oxygen in the setting of acute carbon monoxide poisoning.

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EBEM TEACHING POINT

Quality Assessment. The result of any systematic review depends on the quality of the primary studies included. Cochrane Reviews of therapeutic interventions focus on randomized controlled trials since randomization is the only means of allocation that controls for unknown and unmeasured confounders, as well as those that are known and measured.⁸ Although randomized controlled trials provide the best evidence for medical interventions, they are not immune to bias.⁹ Studies determined to have low methodological quality tend to exaggerate the overall estimate of treatment effect.⁶ In an effort to summarize and compare the internal validity of trials, meta-analysts often report a composite quality score for each study. The Jadad score uses a 5-point scale that is based on descriptions of randomization, blinding, and dropouts or withdrawals.⁶ A composite score may provide a useful overall assessment of quality when comparing trials and may be used in a sensitivity analysis. However, a summary score often does not account for the variation and complexity of clinical trial methodology. Consequently, it has been recommended that the relevant methodologic aspects of each trial be identified and assessed individually.⁹ The authors of this Cochrane Review not only provided an overall estimate of study quality using the Jadad score but also summarized important differences in the internal and external validity among trials. This level of detailed quality assessment allows the clinician to appropriately interpret and apply the results to his or her setting.

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The Emergency Medicine Continuous Certification (EMCC) program replaced the former recertification process starting January 1, 2004. All diplomates who want to maintain their certification with ABEM beyond their current certification expiration date must participate fully in the EMCC program. EMCC has four components that are briefly described below. A full description of EMCC is available on the ABEM website www.abem.org

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