CJEM JOURNAL CLUB

Should hyperbaric oxygen be used for carbon monoxide poisoning?

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Clinical question

Does hyperbaric oxygen therapy (HBO) provide clinical benefit by reducing neurologic sequelae after 1 year for non-pregnant patients presenting with carbon monoxide (CO) poisoning?

Search

A MEDLINE search from 1966–2005. MESH headings:

1.	exp/carbon monoxide poisoning	3114
2.	exp/hyperbaric oxygenation	7481
3.	1 and 2	459
4.	limit 3 to clinical trial	12

Articles chosen

The 12 studies identified by the search were narrowed down to the 5 chosen for discussion here.[1–5] The other 7 studies were either comments, did not measure clinically relevant outcomes, only looked at fetuses or were not clinical trials. A recently published Cochrane review[6] revealed 1 additional article, which we also discuss here.[7]

Objective

To determine if there is evidence of improved clinical outcome during the first 4–6 weeks following treatment with HBO compared with treatment with normobaric oxygen (NBO) for CO poisoning.

Background

Carbon monoxide is an imperceptible gas generated during the incomplete combustion of carbon-based compounds[6] and has an affinity approximately 240 times greater than oxygen for the hemoglobin molecule. Inhaled CO exerts its toxic effect by displacing oxygen and binding to deoxyhemoglobin to form carboxyhemoglobin; by shifting the hemoglobin–oxygen dissociation curve to the left, impairing cellular oxygen delivery; and by interfering with cellular oxygen storage, thus impairing cellular metabolism.

At high concentrations, oxygen competes with CO for hemoglobin binding sites and is therefore a mainstay of therapy for CO poisoning. Carboxyhemoglobin's 4–8-hour half-life falls to approximately 2 hours in the presence of 100% oxygen, and to 30 minutes if 100% oxygen is delivered at 3 atmospheres of pressure. However, despite physiologic rationale supporting the value of HBO therapy, its use in CO poisoning remains controversial and it is typically recommended only for the most severe cases.[8,9] The objective of this review was to determine if there is evidence that HBO improves clinical outcomes more than NBO in patients being treated for CO poisoning.

Populations studied and study design

Table 1 illustrates the settings, population, study designs, interventions, comparison protocol, outcome measures, results, conclusions and limitations of the 6 assessed studies.[1–5,7] All studies evaluated non-pregnant adults.

Results

The studies in this analysis used clinical findings, neuropsychological tests, or the electroencephalogram (EEG) to assess the development of neurologic sequelae. Clinically significant neurologic sequelae were detected using physical examination or self-assessment questionnaires. The neuropsychological tests used to identify neurologic sequelae measured attention, information processing,

Table 1. Characteristics of the 6 studies chosen for assessment

Study characteristic	Weaver et al[1] (*n* = 147)	Scheinkestel et al[2] (*n* = 191)	Ducassé et al[3] (*n* = 26)	Mathieu et al[4] (*n* = 575)	Thom et al[7] (*n* = 65)	Raphael et al[5] (*n* = 915)
Setting and population*	Mid-West EDs (USA)	Australian HBO centre	ICU patients (France)	ED patients (France)	Pennsylvania EDs	ED patients (France)
Study design	RCT. Patients, care givers, statisticians and investigators blinded.	Stratified randomization based on exposure type. Patients and outcome assessors blinded.	RCT. Nonblinded.	RCT. Specific study design not available.	RCT. Nonblinded. Patients advised to contact hospital if symptoms developed.	
Intervention: HBO protocol	Session 1: 100% O_2 at 3 ATA for 50 min then 2 ATA for 55 min Sessions 2–3: 100% O_2 at 2 ATA for 90 min. All within 24 h.	100% O_2 at 2.8 ATA for 60 min daily for 3 d (6 d in "clinically abnormal" patients)	100% O_2 at 2.5 ATA for 2 h then 50% O_2 at 2.5 ATA for 6 h	100% O_2 at 2.5 ATA for 1.5 h	100% O_2 at 2.8 ATA for 30 min then 100% O_2 at 2.0 ATA for 90 min	NBO for 4 h then 100% O_2 at 2 ATA for 1 h or NBO for 2–4 h then 100% O_2 at 2 ATA for 1 h twice in 12 h
Intervention: Comparison protocol	Sham treatment: NBO for equal time period	Sham treatment: NBO for equal daily time period for 3 d	NBO for 6 h then 50% O_2 at 1 ATA for 6 h	NBO for 12 h	NBO until symptoms resolved	NBO for 6 h
Outcome measures	Neuropsychological tests and self-report symptoms at 6 wk, 6 mo and 12 mo	Neuropsychological tests at completion of treatment	Clinical exam at 2 & 12 h, abnormal EEG at 24 h and 21 d	Neuropsychological testing at 1, 3, 6, 12 mo	Neuropsychological tests and symptoms at 1 and 5 wk	Self-assessment survey and physical exam at 1 mo
Results (Number of patients who developed neurological sequelae)	At 6 wk: HBO: 19/76; NBO: 35/76 At 6 mo: HBO: 16/76; NBO: 29/76 At 12 mo: HBO: 14/76; NBO: 25/76 Memory deficit at 6 wk HBO: 21/75; NBO: 37/72 Concentration deficit at 6 wk HBO: 21/75; NBO: 37/72	At end of treatment: HBO: 77/104; NBO: 59/87	At 2 h: HBO: 2/13; NBO: 9/13 At 12 h: HBO: 0/13; NBO: 5/13 Abnormal EEG at 24 h: HBO: 4/13; NBO: 8/13 Abnormal EEG at 21 d: HBO: 0/8; NBO: 6/10	At 1 mo: HBO: 69/299; NBO: 72/276 At 3 mo: HBO: 28/299; NBO: 41/276 At 6 mo: HBO: 19/299; NBO: 26/276 At 12 mo: HBO: 13/299; NBO: 14/276	At 1 wk: HBO: 0/30; NBO: 7/30 At 5 wk: HBO: 0/30; NBO: 4/30	At 1 mo: HBO: 170/411; NBO: 50/148
Conclusions	HBO should be used.	No outcome difference for accidentally poisoned patients treated within 4 h of exposure who required ventilation.	HBO shortens recovery time and reduces delayed functional abnormalities in non-comatose patients with acute CO poisoning.	Fewer CO-induced sequelae at 3 mo in the HBO group, but this difference disappears at 1 yr.	HBO reduces the incidence of delayed neurological sequelae.	Patients who did not lose consciousness can be treated with NBO.
Limitations	Study stopped early. Considerable baseline difference between HBO and NBO groups in terms of duration of CO exposure, cerebral dysfunction on admission, CO level at chamber entry.	Allocation was not concealed. Unusually high number of severely poisoned patients (73%). 54% of patients lost to follow-up at 1 mo.	Clinical outcomes only measured immediately after treatment. Long-term status assessed by cerebral blood flow and EEG — but no clinical correlation. Two NBO patients treated with HBO; 30% loss to follow-up at 3 wk.	Patients were excluded if they were comatose — could indicate more severe poisoning. No description how neurological findings were determined.	Patients were excluded if they experienced a loss of consciousness — could indicate more severe poisoning.	

ED = emergency department; HBO = hyperbaric oxygen; ICU = intensive care unit; RCT = randomized controlled trial; O_2 = oxygen; ATA = atmosphere absolute; NBO = refers to 100% oxygen delivered at normobaric pressure unless otherwise specified; CO = carbon monoxide

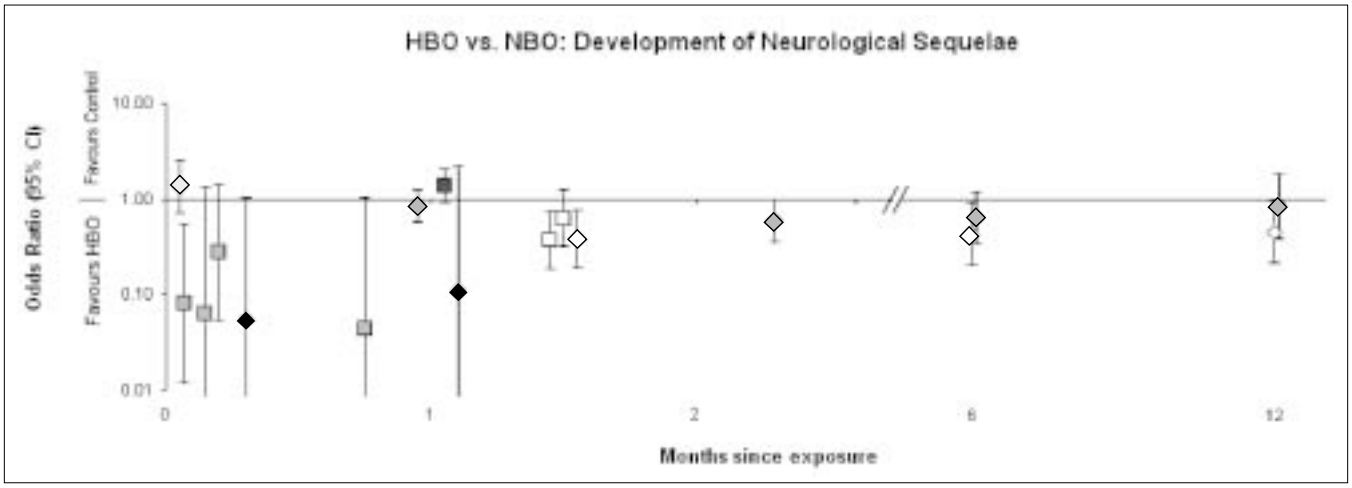

Fig. 1. Neurological sequelae over 1 year for the 6 studies chosen for this assessment. Diamonds = studies that used neuropsychological testing; Squares = studies that used physical examination, self-assessment questionnaires or EEG. White diamonds and squares = Weaver et al[1]; light grey diamond = Scheinkestel et al[2]; dark grey diamonds = Mathieu et al[4]; black diamonds = Thom et al[7]; dark grey squares = Ducasse et al[3]; black square = Raphael et al[5]

memory, learning, reaction time, temporal–spatial orientation, visual discrimination and visual–spatial functioning.

Figure 1 shows key outcomes, stratified by time after exposure.[1–5,7] Results that used neuropsychological tests to determine the presence of neurologic sequelae showed no effect over a 12-month course. Results that used clinical findings showed no effect after 6 weeks.

Comments

The Cochrane reviewers, also using 4–6 weeks as the end point for their analysis, were not able to demonstrate unequivocal benefits for HBO therapy and did not recommend it routinely for CO poisoning. In light of this uncertainty, they recommend that a multi-centre trial be performed to define the role, if any, for HBO therapy in CO poisoning. Examination of all the data points drawn from both strategies over a year reveals that although neuropsychological test scores took up to 12 months to return to normal, the self-reporting of symptoms, clinical assessments and activities of daily living had returned to normal after 6 weeks.

All of the published studies to date have numerous limitations that compromise their validity, including lack of blinding, significant loss to follow-up, HBO therapy at below standard treatment levels, difficulty in interpreting reported results, and exclusion of patients with severe CO poisoning.[10]

With 14 hospital-based HBO chambers in Canada and over 200 in the United States, most of which are single chamber, accessing a hyperbaric chamber for a patient with CO poisoning can be difficult. Even if available, the limited number of facilities means that most eligible patients would require transportation. Furthermore, HBO therapy has potential risks including decompression sickness, cerebral gas embolism, oxygen toxicity, tympanic membrane rupture, sinus barotrauma and pneumothorax.[9]

Even though the Undersea and Hyperbaric Medical Society and others recommend the use of HBO for CO poisoning,[11] a thorough review of the evidence does not support this practice in medicine.

Competing interests: None declared.

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