Hyperbaric oxygen did not reduce persistent neurologic sequelae of carbon monoxide poisoning


Question
In patients with all grades of carbon monoxide (CO) poisoning, is hyperbaric oxygen (HBO) better than normobaric oxygen (NBO) for reducing persistent and delayed neurologic sequelae?

Design
Randomized, double-blind, controlled trial with up to 1-month follow-up.

Setting
A hospital multiplace, hyperbaric chamber in Melbourne, Victoria, Australia.

Patients
191 patients (mean age 36 y; 82% men) who had any grade of CO poisoning (severe CO poisoning 73%). Pregnant women, children, and burn patients were excluded. Follow-up was complete at the end of treatment; 46% of patients were assessed at 1 month.

Intervention
After stratification for poisoning (accidental or suicide) and ventilation (mechanical ventilation or no ventilation), patients were allocated by using cluster randomization to HBO ($n = 104$) or NBO ($n = 87$). Patients in the HBO group received 100% oxygen by hood, occlusive face mask, or mechanical ventilator in the hyperbaric chamber for 100 minutes (60 min at 2.8 atmosphere absolute). Patients in the NBO group received 100% oxygen at 1.0 atmosphere absolute, and the chamber was flushed with air regularly to simulate pressurization. All treatments were given once daily for 3 days, and patients received continuous oxygen, 14 L/min, by nonocclusive face mask between treatments. Patients who were clinically abnormal or had poor neuropsychological outcome after 3 treatments received 3 additional treatments.

Main outcome measures
Persistent neurologic sequelae (poor outcome at hospital discharge) or delayed neurologic sequelae (relapse after discharge) were assessed by using 7 neuropsychological tests: digit span forward and backward and simple reaction and choice reaction time tests on the Wechsler Adult Intelligence Scale, Revised; short-term and long-term free recall tests; and overall score on the Rey auditory verbal learning test.

Main results
More patients in the HBO group than in the NBO group had > 3 treatments (28% vs 15%, $P = 0.01$). After treatment, patients in the NBO group had better scores on the Rey auditory verbal learning test than did those in the HBO group (mean score difference 5.5, 95% CI 1.2 to 9.8). The groups did not differ for the other 6 tests or for persistent neurologic sequelae; the study had > 99% power to detect a 10% difference. Abnormal test results were more frequent in the HBO group than in the NBO group (mean difference in number of abnormal test results 0.7, CI 0.1 to 1.3).

Conclusion
In patients with all grades of carbon monoxide poisoning, hyperbaric oxygen did not reduce persistent neurologic sequelae.

Commentary
CO intoxication, accidental or intentional, is an important cause of poisoning morbidity and mortality. CO mediates toxicity through competition with oxygen for hemoglobin, which results in tissue hypoxia. The feared neuropsychiatric syndrome, a complication of CO poisoning, may result from other mechanisms, including post-ischemic brain reperfusion. Oxygen is key to treatment of CO intoxication because oxygen hastens the dissociation of CO from hemoglobin. However, controversy exists about whether HBO is more efficacious than NBO in reducing neuropsychiatric and other sequelae of CO intoxication. Despite the paucity of high-quality clinical trials showing clear superiority of HBO over NBO for CO-intoxicated patients, HBO is still frequently recommended.

This well-designed trial by Scheinkestel and colleagues compared neurologic sequelae in patients with CO intoxication after HBO or NBO. The NBO regimen was no more than that used in ordinary practice. The study did not show superiority of HBO compared with NBO in any neuropsychological outcome measured, although less than half the patients were assessed at 1 month. The results suggest that in the population studied, HBO is no more effective than NBO.

Ideally, clinical trials comparing HBO with various NBO regimens in patients with CO poisoning would be done to assess a range of clinical outcomes, including delayed neurologic symptoms. However, funding of these trials is unlikely to be feasible. This study shows that NBO in the regimen described is effective for treating CO poisoning. Physicians, particularly the majority who do not have direct access to HBO, can be reassured by this study that they are providing quality care by using NBO oxygen to treat patients with CO poisoning.

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References

Authors' response
Using the treatment protocols described, our study provides no evidence that HBO is more useful than NBO, even if it is available.

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