Outcome of Patients Experiencing Cardiac Arrest With Carbon Monoxide Poisoning Treated With Hyperbaric Oxygen

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Received for publication August 21, 2000. Revisions received November 22, 2000, and January 18, 2001. Accepted for publication March 5, 2001.

Presented at the Undersea and Hyperbaric Medical Society annual meeting, Stockholm, Sweden, June 2000.

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0196-0644/2001/$35.00 + 0
47/1/115532
doi:10.1067/mem.2001.115532

Study objective: We sought to examine the outcome of a subgroup of patients with extreme carbon monoxide (CO) poisoning, specifically those discovered in cardiac arrest, resuscitated, and subsequently treated with hyperbaric oxygen (HBO_2). Opinions of hyperbaric medicine physicians regarding the treatment of such patients were also sought.

Methods: Records of patients treated with HBO_2 for acute CO poisoning at Virginia Mason Medical Center in Seattle from September 1987 to August 2000 were reviewed. Those who were resuscitated from cardiac arrest in the field before HBO_2 treatment were selected for detailed analysis. Patient demographic data and information regarding circumstances of the poisoning, resuscitation, HBO_2 treatment, and subsequent course were extracted and collated. In addition, a postal survey of medical directors of North American HBO_2 treatment facilities regarding opinions about the management and outcome of such patients was performed.

Results: A total of 18 patients were treated with HBO_2 after resuscitation from CO-associated cardiac arrest. They included 10 female and 8 male patients ranging in age from 3 to 72 years. Sources of CO included house fires (10 patients) and automobile exhaust (8 patients). Patient carboxyhemoglobin levels averaged 31.7%±11.0% (mean±SD), and arterial pH averaged 7.14±0.19. Presenting cardiac rhythm was a bradydysrhythmia in 10 of 18 patients. HBO_2 treatment was administered an average of 4.3 hours after poisoning (≤3 hours in 10 patients and ≤6 hours in 15 patients). Despite this, all 18 patients died during their hospitalizations. Medical directors of hyperbaric treatment facilities estimated a 74% likelihood of survival for a hypothetical patient with this presentation.

Conclusion: In this consecutive case series, cardiac arrest complicating CO poisoning was uniformly fatal, despite administration of HBO_2 therapy after initial resuscitation. Survey results suggest that physician education regarding this subset

of CO-poisoned patients is needed. The prognosis of this condition should be considered when making triage and treatment decisions for patients poisoned to this severity.

[Hampson NB, Zmaeff JL. Outcome of patients experiencing cardiac arrest with carbon monoxide poisoning treated with hyperbaric oxygen. *Ann Emerg Med.* July 2001;38:36-41.]

INTRODUCTION

Carbon monoxide (CO) poisoning is a significant health problem in the United States. Although the exact incidence is unknown, one study estimated that more than 40,000 patients are seen annually in US emergency departments for recognized CO poisoning.[1] CO toxicity is mediated by a number of mechanisms,[2] with cardiac and central nervous system manifestations resulting in the most significant morbidity and mortality.

Hyperbaric oxygen (HBO_2) is used to treat some patients with CO poisoning. In 1992, an estimated 2,355 cases were treated with HBO_2 in the United States.[3] Only the most severely poisoned patients are typically selected for treatment with HBO_2.[3] The selection criteria recommended by the Undersea and Hyperbaric Medical Society include transient or prolonged unconsciousness, neurologic signs, or cardiovascular dysfunction.[4] The purpose of this study was to investigate the outcome of patients with the most severe form of cardiovascular dysfunction from CO poisoning, cardiac arrest, when treated with HBO_2 after successful initial resuscitation. In addition, a survey was performed to explore the attitudes of practicing hyperbaric medicine physicians regarding treatment of such patients.

MATERIALS AND METHODS

A departmental log of patients administered HBO_2 therapy for acute CO poisoning at Virginia Mason Medical Center in Seattle from September 1, 1987, through August 30, 2000, was used to identify individuals treated with HBO_2 while mechanically ventilated. ED and hyperbaric department records of those patients were reviewed to identify patients resuscitated from cardiac arrest in the field before hyperbaric therapy. Cardiac arrest was defined for the purpose of this study as discovery of a patient with absence of a detectable pulse, unresponsiveness, and apnea. Data abstracted for such cases included demographic information; circumstances of CO exposure; details of resuscitation, transport, and HBO_2 treatment; and final outcome. Retrospective reviews of this type are exempt from institutional review board approval at our institution.

In addition, a postal survey was mailed in March 2000 to the medical directors of all 317 clinical hyperbaric chamber facilities in the United States, Canada, and Puerto Rico listed in the 1998 Undersea and Hyperbaric Medical Society chamber directory.[5] Medical directors were presented the following clinical scenario:

> A 35-year-old female is accidentally exposed to carbon monoxide from automobile exhaust and discovered unconscious on the garage floor. Paramedics find her pulseless with idioventricular rhythm, heart rate 20 per minute. Following resuscitation in the field, she is transported to your hospital's emergency department. She arrives there intubated, comatose, unresponsive to stimulation, in sinus tachycardia, with blood pressure 100/60. Arterial blood gas analysis demonstrates pH 7.16, P_{CO_2} 29, P_{O_2} 480, and COHb 30.7%. Resuscitation, transport, and emergency department stabilization have taken three hours.

A questionnaire asked whether they would recommend HBO_2 therapy for such a patient and asked them to estimate prognosis.

Simple descriptive statistics were used to report results.

RESULTS

In the 13-year period studied, 980 patients were treated with HBO_2 for severe CO poisoning. Among these, 18 (1.84%) were treated with HBO_2 after they were resuscitated from cardiac arrest in the field, complicating their CO exposure. These included 10 female and 8 male patients ranging in age from 3 to 72 years (mean±SD, 35±17 years; Table 1).

Sources of CO included house fires (10 patients) and automobile exhaust (8 patients). Seven exposures were accidental, 7 were intentional, 1 was homicidal, and 3 were of undetermined intent. Six patients (4 intentional and 2 accidental exposures) were known from toxicology screening to have been associated with exposure to other neuroactive drugs, including ethanol (4 patients), opiates (3 patients), benzodiazepines (2 patients), and tetrahydrocannabinol (1 patient). It was not possible to determine duration of CO exposure from medical record review in most cases.

Each patient's cardiac rhythm at the time of discovery is listed in Table 1. In 10 of 18 cases, patients were found with a bradydysrhythmia, typically described in the medical records as an idioventricular rhythm. The duration of field resuscitation was recorded in available medical records for only 6 patients and ranged from 19 to 45 minutes.

On arrival in the initial ED, most patients (12/18) were described as comatose and unresponsive to stimulation. A minority were described as demonstrating movement in response to stimulation (3/18), some degree of respiratory effort (2/18), or sluggish pupillary response to light (1/18). Presenting carboxyhemoglobin level was available in all patients and ranged from 14.6% to 55.6% (mean±SD, 31.7%±11.0%). ED arterial blood gas values were available for 17 of 18 patients and were notable for severe metabolic acidosis, with an average pH of 7.14±0.19 (mean±SD). Cyanide levels were not obtained in any patients.

Patients were treated in a multiplace hyperbaric chamber while intubated and mechanically ventilated. HBO_2 treatment was initiated 2 to 14 hours after removal from CO exposure, with an average time to treatment of 4.3±2.8 hours (mean±SD). HBO_2 treatment was initiated 3 or fewer hours after discovery in 10 of 18 patients and after 6 or fewer hours in 15 patients. Patients were treated with one of 2 HBO_2 protocols. Six patients treated from 1987 through 1992 received four 23-minute periods of 100% oxygen breathing at 2.8 atmospheres absolute (atm abs) pressure. Twelve patients referred after 1992 were treated with the US Air Force CO protocol.[6] This includes two 23-minute oxygen breathing periods at 3.0 atm abs, followed by two 25-minute oxygen periods at 2.0 atm abs. One patient's HBO_2 treatment was aborted after the initial oxygen period at 3.0 atm abs because of hemodynamic instability. Two of the patients treated with the US Air Force protocol received an additional HBO_2 treatment on the second day of hospitalization. Arterial blood gas measurements were obtained for 17 patients during HBO_2 treatment. Arterial P_{O_2} greater than 760 mm Hg was documented in 15 of 17 patients during HBO_2 therapy. In the remaining 2 patients, acute lung injury caused by smoke inhalation was believed to be the cause for impaired oxygenation.

All 18 patients died during hospitalization (95% CI for the 0% survival rate, 0% to 18.5%). Time from discovery to death ranged from 9 hours to 7 days (median, 42 hours; 25th percentile, 24 hours; 75th percentile, 73 hours). In most cases, medical support was withdrawn after neurology consultation indicated severe, irreversible brain damage. Autopsies were performed in 17 of 18 cases. Causes of death recorded on death certificates by the county medical examiner were "hypoxic encephalopathy" or "anoxic encephalopathy" caused by CO poisoning in all cases.

Results of the survey of medical directors of North American hyperbaric oxygen treatment facilities are shown in Table 2. Responses were received from 150 (47%) facilities. When presented with a description of a case of CO poisoning typical of that seen in this series, 100% of responding medical directors would recommend treatment with HBO_2. They predicted 74% probability of survival after such treatment, with a 28% chance for complete recovery without neurologic sequelae.

Table 1.
Patient data.

Patient No.	Sex	Age (y)	Initial Cardiac Rhythm	COHb	ED ABG (pH; Pco_2; Po_2)	Outcome
1	M	72	Bradydysrhythmia	22.0	Not available	Died
2	M	41	Bradydysrhythmia	24.9	7.09; 23; 507	Died
3	F	45	Bradydysrhythmia	23.8	7.13; 20; 474	Died
4	F	45	Asystole	14.6	6.92; 15; 486	Died
5	F	49	Bradydysrhythmia	20.5	7.45; 23; 533	Died
6	F	5	Bradydysrhythmia	34.0	7.08; 31; 275	Died
7	F	47	Ventricular fibrillation	44.6	7.40; 21; 385	Died
8	M	37	Asystole	34.6	6.98; 47; 371	Died
9	M	31	Bradydysrhythmia	28.7	7.14; 37; 391	Died
10	F	41	Bradydysrhythmia	29.0	7.36; 23; 554	Died
11	F	34	Ventricular fibrillation	28.8	7.30; 29; 502	Died
12	M	3	Unknown (pulseless)	16.5	7.10; 14; 662	Died
13	M	37	Bradydysrhythmia	55.6	7.12; 22; 457	Died
14	F	47	Ventricular fibrillation	34.9	6.99; 39; 532	Died
15	M	5	Bradydysrhythmia	42.0	7.24; 37; 381	Died
16	F	31	Asystole	31.0	7.23; 36; 510	Died
17	M	28	Asystole	35.7	7.09; 44; 662	Died
18	F	33	Bradydysrhythmia	49.5	6.70; 27; 154	Died

COHb, Blood carboxyhemoglobin level; **ABG**, arterial blood gas analysis.

DISCUSSION

Cardiac arrest complicating CO poisoning resulted in 100% mortality in this series, despite initial resuscitation

Table 2.
Opinions of medical directors of North American hyperbaric oxygen treatment facilities regarding management and outcome of patients with CO-associated cardiac arrest (see *Methods section for hypothetical case description*).

Would you recommend HBO_2 treatment for this patient?	Yes 100%	No 0%
If treated with HBO_2, what likelihood would you predict for the following 3 possible outcomes?		
1. Death during hospitalization		26%±23%
2. Survival to hospital discharge with permanent neurologic sequelae		46%±23%
3. Survival to hospital discharge with eventual complete recovery		28%±27%

Values are given as mean±SD where applicable.

in the field with return of spontaneous circulation and subsequent HBO_2 treatment.

A number of studies have documented the poor prognosis of patients with out-of-hospital cardiac arrest in general. Rates of survival to hospital discharge in reported series have ranged from 1.4% to 26%[7-10] and are estimated to average 20% overall.[11] When one examines only those patients who achieve return of spontaneous circulation with resuscitation and are admitted to a hospital, survival rates in the range of 14% to 57% are reported.[7,9,10] A noncardiac cause for arrest has been identified with a poorer prognosis,[12] a factor relevant to all the patients in the present series. Discovery of the arrested patient in asystole or bradydysrhythmia has also been described as associated with a worse prognosis.[7,10] Among the 18 present patients, 4 were discovered in asystole and 10 in bradydysrhythmia.

Several published clinical series have included patients with CO-associated cardiac arrest. Among 5 pediatric patients with cardiac arrest caused by smoke inhalation reported by Suominen et al,[13] none survived. In a series of children with CO poisoning reported by Meert et al,[14] 10 patients were described who presented with cardiopulmonary arrest. Eight died with hypoxic-ischemic encephalopathy, and 2 survived, both with adverse neurologic sequelae. Hantson et al[15] described 10 adult patients admitted to an ICU in Paris, France, with cardiac arrest caused by smoke inhalation, all of whom died. All exhibited high blood carboxyhemoglobin and cyanide levels and died in the critical care unit of "brain failure." A report from Australia on 100 consecutive hospital admissions of adults with CO poisoning mentions that 5 presented with cardiac arrest.[16] The article implies that some may have survived but does not provide treatment information or morbidity data for that subgroup of patients. A large study from Helsinki, Finland, examining out-of-hospital cardiac arrests in that city from 1994-1995 included 5 patients with arrest caused by CO poisoning.[17] Personal communication with the first author of that study reveals that 3 of the 5 died in the field. The other 2 achieved return of spontaneous circulation but died in the hospital. Neither were treated with HBO_2. Their emergency medical system records include an additional 7 patients with CO-associated cardiac arrest in 1993 and 1996-1998, none of whom survived despite return of spontaneous circulation in 2 (M. Kuisma, personal communication, December 13, 1999).

Four previously published series include patients with CO-associated cardiac arrest who were resuscitated and treated with HBO_2. In 2 of the studies, a total of 11 such patients were reported, all of whom died despite HBO_2 therapy.[18,19] The third study described 23 patients treated with HBO_2 after resuscitation from CO-associated cardiac arrest.[20] Seventeen of the 23 died during the hospitalization, 6 of recurrent fatal cardiopulmonary arrests and 11 after the removal of life support systems after diagnosis of brain death. The ultimate outcome of the other 6 patients, including the degree of neurologic recovery, is unknown. The fourth study included 2 patients with cardiac arrest.[21] A patient treated with HBO_2 died, and one treated with normobaric oxygen survived.

It can be seen that cardiac arrest complicating CO poisoning carries a dismal prognosis, even if resuscitation accomplishes return of spontaneous circulation and the patient receives HBO_2 therapy. A number of reasons may be postulated to explain this. First, one must consider the possibility that HBO_2 is in some way detrimental in this group of patients. This seems unlikely in light of the fact that 4 of 6 prospective, randomized clinical trials reported to date comparing normobaric oxygen and HBO_2 treatment for acute CO poisoning of lessor severity have demonstrated benefit from HBO_2.[21-26]

A second possible explanation for poor prognosis might be inadequate HBO_2 treatment. The HBO_2 protocols that were used to treat our patients are standard therapy in the United States.[6] Whether additional repetitive HBO_2 treatments would have altered outcome is unknown. Although some previously published uncontrolled case series have proposed that repetitive treatment of CO-poisoned patients may be beneficial,[16,27] no prospective controlled data have demonstrated a clear benefit of repeat HBO_2 therapy over a single treatment.

It has been previously shown that HBO_2 treatment of CO-poisoned individuals is more effective when delivered within 6 hours of removal from CO exposure.[28] In the present series, more than half of the patients were treated within 3 hours, yet all died. The possibility that even more immediate HBO_2 therapy might be effective exists but seems unlikely.

Another explanation for the high mortality in this subgroup of CO-poisoned patients might be concomitant poisoning with other toxins, particularly cyanide. Among patients poisoned with CO in house fires, many would be expected to have simultaneous cyanide poisoning. This was documented in 100% of patients undergoing cardiac arrest sustaining CO poisoning from smoke inhalation in one report.[15] This does not, however, entirely explain the poor prognosis seen in the present series. Among the 18 fatal poisonings, 8 patients were exposed to CO from automobile exhaust, none of whom

would be expected to have simultaneous cyanide poisoning.

Finally, the poor prognosis may simply be because of the severity of the central nervous system insult that occurs when cardiac arrest complicates CO poisoning. CO toxicity is mediated in part through effects on hemoglobin, which are commonly known as "CO hypoxia."[2] A variety of other mechanisms have also been described. In patients who experience cardiac arrest, the nervous tissue insult is obviously compounded by the absence of oxygen delivery, which occurs when cardiac output ceases. Many of the other biochemical mechanisms of CO toxicity may be amplified by such ischemia. For example, if brain anoxia develops during CO exposure, cytochrome oxidase becomes reduced and CO binds to it without having to compete with oxygen. After the oxygen supply is replenished, the rate of respiration in CO-inhibited mitochondria is restored more slowly than in mitochondria that were exposed to oxygen deprivation alone.[2,29] In another animal model, a period of hypotension was required in addition to CO exposure for CO-mediated brain lipid peroxidation to occur.[30] It would appear that the combination of cardiac arrest with CO poisoning may present an overwhelming insult that is only rarely survivable.

Some limitations of our study should be noted. First, it was a retrospective review without uniform diagnostic entry criteria. As such, it is possible that additional patients referred and treated with HBO_2 also experienced cardiac arrest that was not recorded in their records because it was a less severe event. Such cases could have been missed by our review and might have had a better outcome. The study is also limited by its small size (18 patients). If the next 2 patients with the syndrome were to survive, the survival rate would be 10% and not 0%. A larger study is needed to conclude that HBO_2 therapy for such patients is futile.

All hyperbaric facility medical directors responding to our survey would treat such patients with HBO_2 if they had experienced return of spontaneous circulation with resuscitation and were in their own hospital's ED. This likely relates in part to the fact that no prior studies have been published reporting the dismal outcome of this subgroup of patients in a systematic manner and indicates that physician education is needed. It should be noted, however, that patients in our study did not present initially to our hospital's ED and were referred from an outside ED. This added a component of delay to hyperbaric treatment, and the remote possibility cannot be excluded that HBO_2 therapy delivered even earlier than in this study might be more effective.

On the basis of the present experience and review of the available literature, it must be concluded that cardiac arrest associated with CO poisoning carries an extremely poor prognosis for survival, with or without HBO_2 treatment. This should be taken into consideration when triaging such patients, especially if HBO_2 therapy requires significant transport of these critically ill patients.

Author contributions: NBH conceived the study. NBH and JLZ designed the trial. JLZ performed chart review for data extraction and database entry. NBH performed data analysis and drafted the manuscript. Both authors contributed significantly to its revision. NBH takes responsibility for the paper as a whole.

REFERENCES

1. Hampson NB. Emergency department visits for carbon monoxide poisoning in the Pacific Northwest. *J Emerg Med.* 1998;16:695-698.

2. Piantadosi CA. Diagnosis and treatment of carbon monoxide poisoning. *Respir Care Clin North Am.* 1999;5:183-202.

3. Hampson NB, Dunford RG, Kramer, et al. Selection criteria utilized for hyperbaric oxygen treatment of carbon monoxide poisoning. *J Emerg Med.* 1995;13:227-231.

4. Hyperbaric Oxygen Therapy Committee. In: Hampson NB, ed. *Hyperbaric Oxygen Therapy: 1999 Committee Report.* Kensington, MD: Undersea and Hyperbaric Medical Society; 1999:9-12.

5. *Hyperbaric Chambers, United States and Canada: A Directory of Hyperbaric Treatment Chambers.* Kensington, MD: Undersea and Hyperbaric Medical Society; 1998.

6. Hampson NB, Dunford RG, Norkool DM. Treatment of carbon monoxide poisonings in multiplace hyperbaric chambers. *J Hyperbaric Med.* 1992;7:165-171.

7. Becker LB, Ostrander MP, Barrett J, et al. Outcome of CPR in a large metropolitan area—where are the survivors? *Ann Emerg Med.* 1991;20:355-361.

8. Eisenberg MS, Horwood BT, Cummins RO, et al. Cardiac arrest and resuscitation: a tale of 29 cities. *Ann Emerg Med.* 1990;19:179-186.

9. Lombardi G, Gallagher EJ, Gennis P. Outcome of out-of-hospital cardiac arrest in New York City: the Pre-Hospital Survival Evaluation (PHASE) study. *JAMA.* 1994;271:678-683.

10. Myerburg RJ, Conde CA, Sung RJ, et al. Clinical, electrophysiologic and hemodynamic profile of patients resuscitated from prehospital cardiac arrest. *Am J Med.* 1980;68:568-576.

11. Thel MC, O'Connor CM. Cardiopulmonary resuscitation: historical perspective to recent investigations. *Am Heart J.* 1999;137:39-48.

12. Rogrove HJ, Safar P, Sutton-Tyrrell K, et al. Old age does not negate good cerebral outcome after cardiopulmonary resuscitation: analyses from the brain resuscitation clinical trials. *Crit Care Med.* 1995;23:18-25.

13. Suominen P, Rasanen J, Kivioja A. Efficacy of cardiopulmonary resuscitation in pulseless paediatric trauma patients. *Resuscitation.* 1998;36:9-13.

14. Meert KL, Heidemann SM, Sarnaik AP. Outcome of children with carbon monoxide poisoning treated with normobaric oxygen. *J Trauma.* 1998;44:149-154.

15. Hantson P, Butera R, Clemessy JL, et al. Early complications and value of initial clinical and paraclinical observations in victims of smoke inhalation without burns. *Chest.* 1997;111:671-675.

16. Gorman DF, Clayton D, Gilligan JE, et al. A longitudinal study of 100 consecutive admissions for carbon monoxide poisoning to the Royal Adelaide Hospital. *Anaesth Intensive Care.* 1992;20:311-316.

17. Kuisma M, Jaara K. Unwitnessed out-of-hospital cardiac arrest: is resuscitation worthwhile? *Ann Emerg Med.* 1997;30:69-75.

18. Murphy DG, Sloan EP, Hart RG, et al. Tension pneumothorax associated with hyperbaric oxygen therapy. *Am J Emerg Med.* 1991;9:176-179.

19. Norkool DM, Kirkpatrick JN. Treatment of acute carbon monoxide poisoning with hyperbaric oxygen: a review of 115 cases. *Ann Emerg Med.* 1985;14:1168-1171.

20. Sloan EP, Murphy DG, Hart R, et al. Complications and protocol considerations in carbon monoxide-poisoned patients who require hyperbaric oxygen therapy: report from a ten-year experience. *Ann Emerg Med.* 1989;8:629-634.

21. Scheinkestel CD, Bailey M, Myles PS, et al. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust.* 1999;170:203-210.

22. Raphael JC, Elkharrat D, Jars-Guincestre MC, et al. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet.* 1989;2:414-419.

23. Ducasse JL, Celsis P, Marc-Vergnes JP. Non-comatose patients with acute carbon monoxide poisoning: hyperbaric or normobaric oxygenation? *Undersea Hyperbaric Med.* 1995;22:9-15.

24. Thom SR, Taber RL, Mendiguren II, et al. Delayed neuropsychological sequelae following carbon monoxide poisoning and its prophylaxis by treatment with hyperbaric oxygen. *Ann Emerg Med.* 1995;25:474-480.

25. Mathieu D, Wattel F, Mathieu-Nolf M, et al. Randomized prospective study comparing the effects of HBO versus 12 hours of NBO in non-comatose CO poisoned patients: results of the interim analysis [abstract]. *Undersea Hyperbaric Med.* 1996;23(Suppl):7.

26. Weaver LK, Hopkins RO, Churchill S, et al. Outcome of acute carbon monoxide poisoning treated with hyperbaric or normobaric oxygen [abstract]. *Undersea Hyperbaric Med.* 2001;28(Suppl).

27. Dean BS, Verdile VP, Krenzelok EP. Coma reversal with cerebral dysfunction recovery after repetitive hyperbaric oxygen therapy for severe carbon monoxide poisoning. *Am J Emerg Med.* 1993;11:616-618.

28. Goulon M, Barois A, Rapin M, et al. Carbon monoxide poisoning and acute anoxia due to breathing coal gas and hydrocarbons. *J Hyperbaric Med.* 1986;1:23-41.

29. Brown SD, Piantadosi CA. Recovery of energy metabolism in rat brain after carbon monoxide hypoxia. *J Clin Invest.* 1992;89:666-672.

30. Thom SR. Carbon monoxide-mediated brain lipid peroxidation in the rat. *J Appl Physiol.* 1990;68:997-1003.