

Carbon Monoxide Exposure Associated with High-risk Features and Intentional Exposure are Infrequently Treated with Hyperbaric Oxygen

Renee L Riggs¹, Frederick W Fiesseler^{2*}, Neeraja Kairam³, Lisa Reedman³, Dave Salo³ and Richard Shih³

¹Department of Emergency Medicine, UMDNJ-Robert Wood Johnson Medical School at New Brunswick, USA

²Atlantic Hyperbaric Associates, Morristown New Jersey, USA

³Department of Emergency Medicine, Morristown Medical Center, USA

*Corresponding author: Frederick Fiesseler, DO, Department of Emergency Medicine Morristown Medical Center, 100 Madison Avenue, Morristown, NJ 07960, USA, Tel: 973-903-8919; E-mail: ffiesseler@yahoo.com

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Abstract

Data is conflicting regarding the management of carbon monoxide (CO) poisoned patients.

Objective: To determine the emergency department management (ED) of intentional CO poisoned patients regarding hyperbaric oxygen therapy (HBO2), compared to those who are unintentionally exposed.

Methodology

Design: A multi-center retrospective emergency department cohort study.

Population: Consecutive patients presenting to 23 Northeastern United States hospital emergency departments, comprising academic, non-academic, urban, suburban, and rural hospitals with the International Classification of Disease primary diagnosis of "toxic effects CO". Patients were "a priori" divided into intentional/unintentional and "high-risk" (syncope, serum carboxyhemoglobin level $\geq 20\%$, change in mental status, cardiac arrest, and/or seizures) or "low-risk" (without the above).

Results: "Toxic effects of CO" was diagnosed in 1136 patients, 1026 charts were available for analysis and 52 (4.8%) met inclusion criteria as intentional. Mean age was 40 years (standard deviation (SD) ± 13), for intentional patients. Overall, high risk intoxication was reported in 12% (N = 124/1026) of patients, compared to 50% (N = 26/52) of the intentional patients ($p \leq 0.0001$). Mean overall CO level was 7%, compared to an intentional rate of 17% ($p \leq 0.0001$). Fifty percent of intentionally exposed high-risk patients received HBO2, while only 36% (N = 45/124) of high-risk patients overall did ($p = 0.27$).

Conclusions: Carbon monoxide poisoned patients with intentional exposures and high-risk clinical features are not more likely to receive HBO2.

Introduction

Carbon monoxide (CO) poisoning is the most common cause of toxicological related death in America and worldwide. Between 2000-2009, the National Poison Data System, reported 68,316 CO exposures representing 0.29% of all poison exposure cases [1]. Carbon monoxide exposures comprise 0.02-0.05% of emergency department (ED) visits [2,3]. An important subset of CO exposure patients are those that are intentional. This patient population is speculated to have more co-ingestants, have a greater likelihood of high-risk exposures, have psychiatric illness obscuring subtle CO effects, and have a delayed presentation. Historical data in such patients is often inaccurate, also [4]. All these factors contribute to the complexity of assessing and managing such patients.

Neurological sequela is one of the most dreaded complications related to this toxin [5-7]. A multi-center randomized blinded study reported hyperbaric oxygen therapy to be beneficial in preventing persistent neurological sequelae following carbon monoxide exposure,

with a number needed to treat of six [8]. Carbon monoxide's toxic effects are thought to be related to: decreased carrying capacity of oxygen with a leftward shift in the oxyhemoglobin dissociation curve, lipid peroxidation, inhibition of oxidative phosphorylation, and direct myoglobin injury.

Our null hypothesis is that intentional CO poisoned patients receive hyperbaric oxygen therapy more frequently, than those who are not. This study also sought to determine if differences in management of unintentional versus intentional exposures occurred. Specifically, a comparison of the high-risk patient subgroup treatments was analyzed.

Methodology

Design

This was a multi-center retrospective ED cohort study.

Population

It comprised of twenty-three emergency departments in Northeastern United States including academic, non-academic, urban, suburban, and rural hospitals. Six of the contributing hospitals perform hyperbaric oxygen therapy (HBO2). Consecutive patients with the International Classification of Disease (ICD-9) primary diagnosis of intentional “toxic effects of CO,” from January 2000 to December 2006 were enrolled.

Protocol

Patient demographic data was compiled in an Excel (Microsoft, Redmond, WA) spreadsheet. “A priori” patients were divided into four groups: “high-risk” (syncope, serum carboxyhemoglobin level \geq 20%, changes in mental status, cardiac arrest, and/or seizures), “low-risk” (without the above), intentional exposure and unintentional exposure. The above criteria have previously been shown to be markers of disease severity [9].

Statistics

Statistical data was performed utilizing a two-tailed Fisher Exact Test and Mann-Whitney, with a preset alpha of 0.05 for significance where appropriate.

A board certified/eligible Emergency Physician or Pediatric Emergency Physician participated in the care of all participants. Medical evaluations were performed as per the discretion of the treating physician. All charts with ICD-9 diagnosis of “carbon monoxide” were extracted using an electronic charting system via web Emergency Medicine Analysis and Reporting System Data Services (eMARS). A manual chart review was then performed by two independent physicians after charts were blinded for personal identifiers. Exclusion criteria included: incorrect ICD9 diagnosis, primary treatment by non-emergency medicine physicians, and chart unavailability. If a disagreement existed regarding mechanism, a third physician made the final determination. The institutional review board approved this study.

Results

Toxic effects of CO were diagnosed in 1136 patients. Of these 1026 (90.3%) charts were available for analysis. Fifty-two patients (5%) met inclusion criteria as intentional exposures. Fifty-one of the patient exposures occurred from auto exhaust, the remaining one via a charcoal briquette fire. Mean age of intentional exposures was 40 years (standard deviation (SD) \pm 13), compared with an overall mean age of 30 years (SD \pm 20). Sixty-six percent of intentional exposures were male, and compared with an overall female predominance of 59% (Table 1).

Characteristics of intoxicated patients	Types of intoxication			
	Intentional	Overall ¹	Intentional high risk	Overall high risk
Total number of males and females	52	1026	26	124

Mean age (years)	40	30	41	40
Number of females (%)	18 (34)	603 (59)	8 (31)	40 (32)
Number of patients admitted/transferred (%)	28/10 (73)	91/33 (12)	18 (69)	76 (61)
Number of “High risk” patients ² (%)	26 (50)	124 (12)	26	124
Number of HBO2 therapy (%)	12 (23)	56 (5)	13 (50)	45 (36)
Number of EKG recorded (%)	29 (56)	182 (18)	16 (62)	76 (61)
Number of arterial blood draw (%)	26 (48)	241 (23)	16 (62)	58 (47)
Number of use of serum cardiac markers (%)	10 (19)	61 (6)	6 (23)	26 (21)
Number of patients with repeat COHb (%)	10 (19)	74 (7)	6 (23)	32 (26)
Mean COHb	17%	7%	26%	22%

Table 1: Characteristics of intentional and unintentional carbon monoxide intoxicated patients.

¹Intentional and unintentional (i.e. accidental) intoxications.

²Carboxyhemoglobin level higher than 20%, syncope, change in mental status, cardiac arrest, and/or seizures.

COHb: Serum Carboxyhemoglobin level; HBO2: Hyperbaric Oxygen Therapy; EKG: Electrocardiogram; N: Number of individuals.

Mean CO level was 7% (95% CI = 0-20) overall, compared to the intentional exposure level of 17% (95% CI = 1-33%) ($p \leq 0.0001$). With regard to intentional exposures: admission occurred in 73% of patients with 61% being admitted to a psychiatric floor. Of admitted intentional patients, those with medical admissions had a mean CO level of 13% (95% CI = 2-24%) compared to a level of 18% (95% CI = 10-26%) in those admitted to psychiatry.

High-risk intoxication was reported in 12% (N = 124/1026) of patients, and comprised 50% (N = 26/52) of the intentional patients ($p \leq 0.0001$). Etiology for intentional high-risk stratification included: elevated CO level (N = 14), syncope (N = 17), cardiac arrest (N = 3), change in mental status (N = 4) and seizures (N = 2). Intentional high-risk patients had a co-ingestion rate of 25%, which was identical to the low-risk intentional group. Three patients died while in the ED overall, all within the intentional high-risk group, with a mean CO level of 52%.

Overall, high-risk patients, had an electrocardiogram (EKG) assessed 61% (N = 76/124) of the time, versus 62% (N = 16/26) in the intentionally exposed group ($p = 1$). Overall, twenty-one percent (N = 26/124) of high-risk patients had cardiac serum markers reported, compared to an intentional rate of 24% ($p = 0.80$).

Of intentional patients, oxygen therapy was initiated in 91%, with 16% requiring intubation. Overall, 36% (N = 45/124) of high risk

patients received HBO2 compared with an intentional rate of 50% (p = 0.27) (Table 2).

Baseline characteristics in intoxicated patients	Mean age (years)	Male gender (%)	Mean COHb (%)	Intubation (%)
Intentional HBO2 therapy	38	70	22	4
Unintentional HBO2 therapy	40	68	22	6
Intentional NMBO2 therapy	40	56	14	12 (50% died)
Unintentional NMBO2 therapy	32	44	7	1
Intentional, no O2	35	70	5	0
Unintentional, no O2	24	42	2.5	0

Table 2: Baseline characteristics based on treatment in carbon monoxide intoxicated patients.

HBO₂: Hyperbaric Oxygen Therapy; NMBO₂: Normobaric Oxygen Therapy; O₂: Oxygen; COHb: Serum Carboxyhemoglobin Level

Discussion

Utilization of HBO2 in CO poisoned patients while remaining controversial is thought to be most beneficial in high-risk patients. In fact, the latest “Cochrane Collaboration” authors conclusion states, “Existing randomized trials do not establish whether the administration of HBO2 to patients with carbon monoxide poisoning reduces the incidence of adverse neurologic outcomes. Additional research is needed to better define the role, if any, of HBO2 in the treatment of patients with carbon monoxide poisoning” [10]. Conversely, Weaver gave HBO2 therapy for CO poisoning a level of evidence of “A” (Meta-analysis of randomized controlled trials) and a class recommendation of IIa (weight of evidence/opinion is in favor of usefulness/efficacy) in his review of the subject [11]. This study found that only 36% of high risk patients received HBO2 therapy compared to 50% (not statistically significant) of high risk intentional exposure cases.

Intentional CO exposed patients may have subtle neurological deficits overlooked because of underlying psychiatric confounding factors (attention, concentration, and affect disorders), and poor cooperation. In these patients the threshold for treatment may need to be lowered. Conversely, one could intuit that if co-ingestions are present causing clinical symptoms such as alteration in mental status, a higher threshold for treatment may be utilized. Unfortunately, little information is available regarding this issue and more research is required to determine which intentionally overdosed patients would benefit most from this therapy and the effects of co-ingestions on treatment protocols.

A significant number of patients that are seen in the emergency department comprise CO exposure. Our intentional CO exposure rate of 4.8 percent was far less than that of Weaver 31% and Scheinkestel 69% [8,12]. This study depicts the incidence of patients presenting to the ED, while most prior studies represent subjects referred from other institutions for HBO2, a different patient population. Hampson also demonstrated an intentional source of CO poisoning of 35% in those

patients treated at their facility, again this depicts a different subset from our ED population [13]. Most prior studies regarding intentional CO exposure and treatment depict those referred for HBO2 therapy and not those presenting to the ED.

HBO2 while thought to be beneficial is not without potential deleterious consequences. Confounding factors such as: availability, oxygen toxicity, barotrauma, risk of transport, and cost need to be tabulated. Each individual patient needs to be evaluated uniquely as to his/her risk stratification regarding these factors. Data remains conflicted regarding the management of carbon monoxide (CO) poisoned patients [8,12,14-18].

The cardiovascular system, a primary organ system susceptible to injury, was examined with EKG or cardiac serum enzymes in only 61% of high-risk patients. Historically, thirty percent of severely exposed patients demonstrate abnormal EKG’s and 35% have abnormal cardiac markers [19]. Henry also demonstrated an incidence of abnormal cardiac markers/kg of 37% in HBO2 treated patients. Importantly, patients with elevated cardiac serum markers had a hazard ratio of 2.1 of dying (p=0.009) [20]. Patients with high-risk CO intoxication should have EKG and cardiac marker testing. Our data suggests that less than adequate cardiac assessment is occurring in these patients.

Three patients in our study had cardiac arrest in the ED. All three patients ultimately died. Short-term mortality is only one concern regarding this disease process. Long-term increased mortality rates among survivors of CO poisoning has also recently been appreciated. Hampson reported on 162 subject deaths in long-term follow-up, while the expected number was only 87. Most of the excess mortality was in the group treated for intentional poisoning. Both short and long-term mortality is a concern in intentionally intoxicated patients [13].

Lastly, our study is not without limitations. Weaver demonstrated that greater than half of those patients with severe CO intoxication develop symptoms of persistent neurological sequelae [8]. Unfortunately, our study was unable to assess neurological sequelae. Physicians need to be more cognizant of the potential for persistent/delayed neurological sequelae and the utility of HBO2. As with all retrospective studies, important information is often not collected or recorded. Inaccuracy of data secondary to patient/ physician inaccuracies can also occur. One could speculate that our large study population limits these effects. In addition, patient morbidity and mortality outcomes data was not available. Further studies are needed to determine why some patients are referred for HBO2 therapy while others are not. Standardized evidence based treatment and referral protocols might be beneficial. It is possible that patients who would likely benefit from this treatment are not being referred for such care.

Conclusion

Carbon monoxide poisoned patients with intentional exposures and high-risk clinical features are not significantly more likely to receive HBO2 therapy.

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