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Original Contribution

Carboxyhemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture?☆

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Abstract

Objective: It is commonly written that carboxyhemoglobin (COHb) measurements correlate with the clinical presentation of patients poisoned with carbon monoxide (CO). However, the evidence supporting this concept is scanty. The present study was performed to analyze COHb measurements in a large population of patients with CO poisoning to determine whether clinically significant correlates exist.

Methods: Records of all patients treated with hyperbaric oxygen for acute CO poisoning at a single private academic medical center from 1978 to 2005 were reviewed. The COHb measurements were analyzed with regard to sex, age, source of CO, loss of consciousness, endotracheal intubation, arterial pH, and death.

Results: Data from 1603 CO-poisoned patients were reviewed, and 1407 were included in the final analysis. Statistically higher COHb measurements were associated with male sex (24.2% ± 11.2% vs 21.5% ± 11.6), adult age range (24.0% ± 11.0% vs 19.5% ± 10.3%), poisoning by CO from fires (25.7% ± 12.1%) or motor vehicles (22.7% ± 24.7%), loss of consciousness (24.3% ± 12.2% vs 22.3% ± 9.4%), lower arterial pH, and death (32.1% ± 12.8% vs 23.1% ± 0.9%).

Conclusions: Despite the fact that statistically significant differences in average COHb measurements were seen with regard to a number of variables, the clinical significance of these differences appeared to be minimal. Moreover, the utility of COHb measurements as predictors of clinical status in CO poisoning was not apparent. At least in part, this likely relates to delay and interval oxygen administration before obtaining COHb measurements.

1. Background

Carbon monoxide (CO) poisoning is common in the United States, accounting for an estimated 50 000 emergency department visits for diagnosed cases annually [1]. Because the signs and symptoms of CO poisoning are nonspecific, it is likely that many more cases are unsuspected or attributed to other etiologies and therefore go undiagnosed. Elevated blood carboxyhemoglobin (COHb) measurements are used to confirm a clinical diagnosis of exposure to CO and, in some instances, assess the severity of poisoning.

When CO poisoning is suspected clinically, measurement of blood COHb is typically performed. An elevated COHb level (>2% for nonsmokers and >9% for smokers) [2] strongly suggests exposure to exogenous CO and supports a

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clinical diagnosis of CO poisoning. Many feel that the degree of elevation of COHb level does not correlate well with the patient's presenting clinical picture and do not use it to direct management. In his review article on the diagnosis and treatment of CO poisoning, Piantadosi wrote, "In general, however, the correlation between clinical deficits and measured COHb level is quite weak" [3]. The Undersea and Hyperbaric Medical Society recommends hyperbaric oxygen therapy for CO-poisoned individuals based upon the clinical severity of illness irrespective of the degree of elevation of their COHb measurements [4].

On the other hand, many articles on CO poisoning contain tables or charts relating degree of COHb elevation to specific symptoms or signs and the severity of the poisoning episode. In their review article on clinical CO poisoning, Ilano and Raffin wrote, "…in general, the severity of the observed symptoms correlates roughly with the observed levels of COHb…" [5]. The Merck Manual Professional Edition states that "Symptoms tend to correlate well with the patient's peak blood carboxyhemoglobin levels" [6].

The predictability of symptoms and signs with specific COHb measurements is clearly a matter of dispute. The present study was conducted to review the clinical characteristics of a large population of patients with acute CO poisoning to determine whether the degree of elevation of the blood COHb level has identifiable clinically significant correlates.

2. Methods

After approval by the institutional review board, records of all patients treated with hyperbaric oxygen for acute CO poisoning at a single medical center from 1978 to 2005 were reviewed. They were identified, and basic information was obtained about each through the use of an institutionally approved database containing all CO-poisoned patients treated in the facility since its inception. Additional information was extracted when necessary from the patients' medical records.

A *case* was defined as an individual treated with HBO_2 with a history of CO exposure, symptoms consistent with CO poisoning, and an elevated blood COHb level (>2%). The COHb measurements reported represent the initial measurement obtained, either during primary workup at an outside facility or after referral to the Virginia Mason Medical Center, resulting in a variable amount of time and oxygen treatment between CO exposures and sampling of blood for COHb measurement. Criteria used to advise hyperbaric treatment of a patient with CO poisoning typically included transient or prolonged unconsciousness, neurologic signs, cardiovascular dysfunction, severe acidosis, or elevation of COHb level to the range of 25%.

Demographic data including first and last name, middle initial, date of birth (DOB), social security number (SSN), sex, race/ethnicity, and intent and source of exposure were extracted from the charts by the 2 authors using a standard data collection tool. Also extracted were clinical data including initial COHb level, initial arterial pH, history of loss of consciousness (LOC), and presence of endotracheal intubation during hyperbaric oxygen treatment.

Although it is recognized that presenting COHb measurements may be normal in CO-poisoned patients because of delay in obtaining a blood sample after removal from the source of exposure and/or interval oxygen administration, patients with COHb measurements less than 2.0% were excluded to ensure that all patients evaluated were indeed exposed to CO.

An application was submitted to the National Center for Health Statistics of the Centers for Disease Control and Prevention to query the National Death Index (NDI) to obtain mortality information about the patients. The NDI is a central computerized index of death record information on file in state vital statistics offices [7]. It is available to investigators only for medical and health research. After approval of an NDI application by the National Center for Health Statistics, a space-delimited text file containing the patients' demographic information including first and last name, middle initial, SSN, DOB, sex, and race was submitted according to NDI protocol. The NDI search criteria specify that each patient record must contain at least one of the following combinations of data items: (1) first and last name and SSN, (2) first and last name and month and year of birth, and (3) SSN and date of birth and sex. Patients for whom neither SSN nor DOB could be obtained were excluded from the study because of the inability to search for their death information according to NDI criteria. By mid-2007, search results were only available for the years 1979 through 2005, limiting analysis to patients who had been treated through December 2005.

The mortality information obtained from the NDI Plus search was used to identify individuals who died within 30 days of the date of treatment. Those deaths were attributed to the CO poisoning episode for the purposes of this study.

Data analysis included summary statistics and linear regression (MedCalc software Version 9.3.3.0 Mariakerke, Belgium). In some analyses involving LOC, intentionally exposed patients were excluded because of the potential for coingestion of other substances, which might be confounding.

3. Results

From 1978 to 2005, a total of 1603 patients were treated with hyperbaric oxygen for acute CO poisoning. Of those, 164 were excluded because their records did not contain an initial documented COHb level greater than 2.0%. An additional 32 patients were excluded because their records contained insufficient demographic information to submit to an NDI search. The study population thus included 1407 patients, representing 88% of the total treated.

Most patients (66%) were male. The average age for the included group was 35 ± 19 years (mean ± SD; range 0-92 years). Intent of poisoning was accidental in 972 (69%), intentional in 427 (30%), and indeterminate in 8.

Common sources of CO included motor vehicle exhaust, 567 (40%); fire, 174 (12%); indoor use of charcoal briquettes, 158 (11%); furnaces, 85 (6%); boats, 84 (6%); forklifts, 82 (6%); gasoline-powered electrical generators, 69 (5%); and propane-burning appliances, 64 (5%) (Table 3).

The COHb measurements for the study population and various subgroups are shown in Table 1. Average COHb level for the entire population was 22.3% ± 11.0% (mean ± SD; range, 2.1%-72.3%). Measurements were slightly but statistically significantly higher for male vs female patients, adults vs pediatric patients (younger than 18 years), and patients experiencing LOC vs those not. The COHb measurements were also significantly higher among the 37 patients who died within 30 days of poisoning as compared with those who survived. Of the decedents, 30 died within the first 72 hours after presentation. The remaining 7 died from 7 to 28 days later.

Table 2 shows occurrence of LOC according to various measurements of COHb in accidentally poisoned patients. Occurrence of LOC was highest at the upper end of the COHb range, but exceeded 40% at all ranges of COHb. Note that 291 patients with intentional poisoning and LOC were not included in this analysis for reasons previously stated.

Emergency department presenting arterial blood gas analysis results were available from 823 patients (58%). Arterial pH ranged from 6.70 to 7.71 (mean, 7.38 ± 0.11).

Table 1 Carboxyhemoglobin measurements for various subgroups of patients

	n	COHb %	COHb %
		Mean ± SD (95% CI of the mean)	Range
All patients	1407	22.3 ± 11.0 (22.7-23.9)	2.1-72.3
Male	922	24.2 ± 11.2 (23.5-24.9)	2.1-72.3
Female	485	21.5 ± 11.6 (20.6-22.5)	2.1-60.0
<18 y old	228	19.5 ± 10.3 (18.2-20.8)	2.2-57.6
≥18 y old	1179	24.0 ± 11.0 (23.4-24.7)	2.1-72.3
Accidental poisoning	972	22.8 ± 10.3 (22.2-23.4)	2.2-64.0
Intentional poisoning	427	23.4 ± 12.4 (23.2-26.6)	2.1-72.3
Unknown intent	8		
LOC	745	24.3 ± 12.2 (23.3-25.1)	2.1-72.3
No LOC	661	22.3 ± 9.4 (21.5-23.0)	2.2-61.0
Unknown	1		
Endotracheal intubation	247	24.8 ± 13.2 (23.0-26.3)	2.1-60.8
Not intubated	1160	23.0 ± 10.5 (22.4-23.6)	2.2-72.3
Died (<30 d)	37	32.1 ± 12.8 (27.9-36.4)	3.0-60.0
Survived (>30 d)	1370	23.1 ± 10.9 (22.5-23.6)	2.1-72.3

CI indicates confidence interval.

Table 2 Incidence of LOC among 972 patients with accidental CO poisoning and referred for hyperbaric oxygen treatment, according to initial COHb measurement

COHb measurement (%)	Incidence of LOC
0-9	55/116 (47%)
10-19	106/253 (42%)
20-29	167/381 (44%)
30-39	92/166 (55%)
>40	39/56 (70%)

Fig. 1 demonstrates the relationship between initial arterial pH and COHb measurements.

4. Discussion

Although this group of approximately 1500 patients only represents a subset of the general CO-poisoned population, their data make clear the fact that generalizations about the relationship of COHb measurements to the clinical presentation of CO poisoning are likely to be inaccurate.

Indeed, COHb measurements were significantly associated with a number of demographic and clinical variables. Measurements were statistically higher in male as compared with female patients, adults as compared with children, individuals experiencing LOC, individuals with lower arterial pH, and individuals who died of their poisoning episode. Blood COHb measurements were also higher in individuals poisoned by exposure to CO from fires or motor vehicles.

However, the clinical significance of these statistically significant differences is questionable. Although some authors have written that symptoms and signs correlate with COHb measurements, the current data would seem to counter that concept. In the present study, clinical findings that are objective and quantifiable were examined. Symptoms such as headache, nausea, or dizziness were not extracted from chart review because of their subjective nature and concern that their recording in the medical record would be variable unless a standardized questionnaire had been used.

On the other hand, LOC is an excellent sign to examine with regard to relationship to COHb measurements. It is obvious to observers when LOC occurs, and the occurrence is likely to be recorded in the record when reported. Although patients experiencing LOC had statistically significantly higher COHb measurements on average, the differences were trivial from a clinical standpoint (24.3% vs 22.3%). It is difficult to imagine a clinical setting where differences of this magnitude could have any implications. Furthermore, the overlap of COHb measurements in those accidentally poisoned and experiencing or not experiencing LOC extended over the entire range of measurements (Table 1). Many patients who experienced LOC had

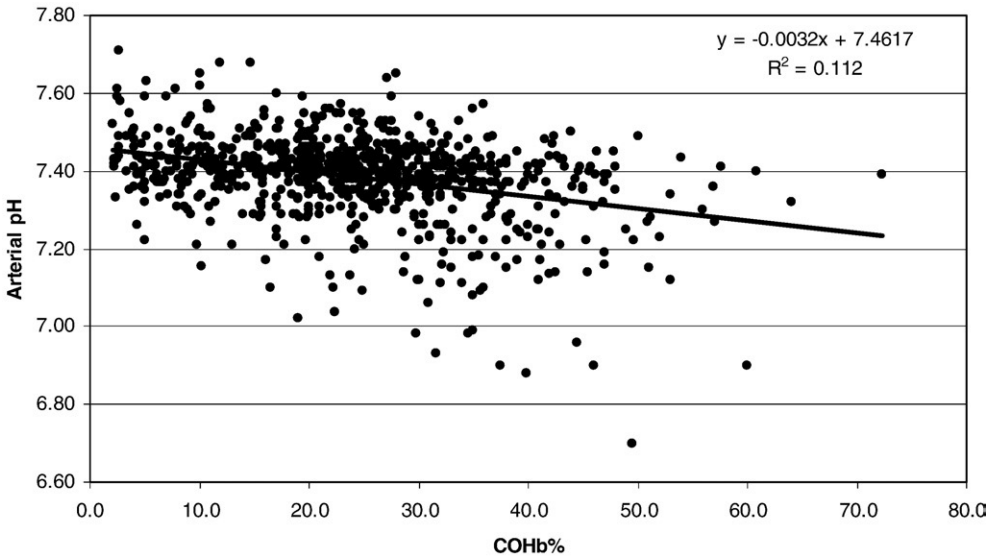

Fig. 1 Initial arterial pH versus initial carboxyhemoglobin (COHb) level in 824 patients with CO poisoning.

presenting COHb measurements less than 10%, and many others who did not lose consciousness had measurements greater than 50%.

In a typical table describing the relationship of symptoms to COHb measurements, syncope is said to be "commonly found" with measurements of 40% to 50% [5]. Among accidentally poisoned patients in this study, the incidence of LOC rose with COHb measurements greater than 30% and rose further with measurements greater than 40% (Table 2). However, LOC occurred with a frequency greater than 40% at all measurements of COHb.

Analysis of arterial pH yields findings similar to those seen with LOC. Although the correlation between increasing COHb level and decreasing pH was significant (Fig. 1), it would be impossible to predict the pH from the COHb level in the clinical setting. Among patients with COHb measurements less than 20%, arterial pH ranged from 7.02 to 7.71. Among patients with COHb measurements greater than 50%, arterial pH ranged from 6.90 to 7.49. Metabolic acidosis is known to result from impaired systemic oxygen delivery due to COHb formation. The variation seen here is further evidence that COHb formation is not the only mechanism of CO toxicity and that other disturbances of cellular energy metabolism may occur [3]. In addition, cardiovascular dysfunction and seizure activity resulting from CO exposure could play a role. A potential limitation is the lack of availability of arterial PCO_2 or serum bicarbonate in our database. Although we presume that most acidosis is metabolic in CO poisoning, a contribution of a respiratory component is certainly possible.

Mortality was associated with the greatest absolute differences in COHb measurements seen in this study. Those who died had average COHb measurements approximately 50% higher than survivors (32.1% vs 23.1%). The range of COHb measurements among individuals who died, however, was wide and inconsistent with the concept that there is a predictable level at which death occurs. Not only did individuals die with initial measurements as low as 3%, but the individual with the highest COHb level (72.3%) survived. Death in patients with extremely low measurements is undoubtedly a function of delay in obtaining blood after the exposure ends, as will be discussed. At the other extreme, however, among the 27 individuals with measurements 50% or higher, 3 died and 24 survived. Although this may be a higher rate of death than is seen at lower COHb measurements, it is certainly not a useful predictor in the individual clinical situation.

A limitation of the study is referral bias. This population sample consists of those considered more seriously ill. Because LOC and COHb measurements greater than 25% were independent criterion for referral for hyperbaric treatment, the population of those patients with LOC may include more individuals with low COHb measurements than normally occurs. Likewise, there may be excess representa-

Table 3 Carboxyhemoglobin measurements for major sources of CO

Source	n	COHb %	COHb %
		Mean ± SD (95% CI of the mean)	Range
Boat	81	23.3 ± 8.7 (21.0-26.3)	3.3-42.7
Charcoal	148	20.8 ± 9.0 (19.4-22.2)	3.0-57.0
Fire	174	25.7 ± 12.1 (23.9-27.5)	2.3-57.6
Forklift	82	23.2 ± 8.4 (21.3-25.1)	3.4-47.3
Furnace	85	21.2 ± 9.8 (19.1-23.3)	2.2-42.3
Generator	69	23.0 ± 10.6 (20.4-25.5)	6.6-49.7
Motor vehicle	567	23.7 ± 12.3 (22.7-24.7)	2.1-72.3
Propane appliance	65	20.4 ± 8.9 (18.1-22.6)	4.1-42.4

tion by individuals with minimal symptoms and marked elevation of COHb measurements. These situations, however, serve to provide numerous examples contrary to the commonly described relationships between COHb and clinical presentation.

Because the differences in COHb measurements between various groups are small, even when statistically significant, and the comparative ranges of COHb measurements overlap so greatly, one must agree with Piantadosi that measured blood measurements correlate weakly with clinical deficits [3]. It is probable that a major reason for this is the delay from termination of the CO exposure to the time blood is drawn for COHb measurement, as well as intervening administration of oxygen. Both allow the COHb level to fall before blood is obtained. Almost all patients had COHb measured at an outside hospital before referral, but information was lacking as to the time lapsed from removal from CO exposure to obtaining blood. Although venous blood drawn into a heparinized sample tube at the scene and transported with the patient for subsequent analysis will remain stable even at room temperature [8], this is not commonly done.

A handheld pulse CO oximeter was recently marketed that allows rapid noninvasive measurement of COHb in addition to conventional pulse oximetry variables [9]. When first responders such as firefighter and emergency medical technicians have this device readily available in the future, it may be found that immediately measured COHb measurements correlate better with symptoms or signs because they are closer to peak measurements. At present, it can simply be said that although elevated COHb measurements are indicative of CO exposure, they frequently do not correlate with poisoning severity.

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