Carbon monoxide (CO) poisoning is common in the United States, accounting for approximately 2,700 deaths annually. Few publications have described the mortality rate of CO-poisoned patients who survive to reach a hospital and die despite maximal medical care. Further, while risk factors for cognitive sequelae in survivors of CO poisoning have become clearer recently, factors associated with death are less well defined. This study was conducted to 1) determine the short-term mortality risk for patients treated with hyperbaric oxygen for CO poisoning, and 2) determine whether any factors related to the poisoning episode are predictive of mortality.

Objective: Carbon monoxide (CO) poisoning is common in the United States, accounting for approximately 2,700 deaths annually. Few publications have described the mortality rate of CO-poisoned patients who survive to reach a hospital and die despite maximal medical care. Further, while risk factors for cognitive sequelae in survivors of CO poisoning have become clearer recently, factors associated with death are less well defined. This study was conducted to 1) determine the short-term mortality risk for patients treated with hyperbaric oxygen for CO poisoning, and 2) determine whether any factors related to the poisoning episode are predictive of mortality.

Design/Setting/Patients: A departmental database and medical records of 1,505 consecutive patients treated with hyperbaric oxygen at a single institution from 1978 to 2005 were reviewed.

Measurements: Demographic and clinical data were extracted for analysis. Mortality data, including cause of death, were obtained through a search of the National Death Index of the National Center for Health Statistics.

Main Results: A total of 38 patients experienced short-term mortality from their episode of CO poisoning, yielding a death rate of 2.6% in medically treated patients. Characteristics significantly associated with mortality included fire as a source of CO, loss of consciousness, carboxyhemoglobin level, arterial pH, and presence of endotracheal intubation during hyperbaric treatment.

Conclusions: The mortality rate for medically treated CO-poisoned patients in this series was 2.6%, similar to the limited combined experience previously reported in the literature. Factors most strongly associated with mortality were severe metabolic acidosis and need for endotracheal intubation. (Crit Care Med 2008; 36:2523–2527)

Key Words: carbon monoxide; poisoning; mortality; cause of death; hyperbaric oxygen
treated CO poisoning is believed to be poorly defined.

The present study was undertaken to investigate the issues of short-term mortality in a large population of CO-poisoned patients treated at one medical center over three decades. We sought 1) to determine the short-term mortality risk for patients treated with hyperbaric oxygen for acute CO poisoning, and 2) to determine whether any factors related to the poisoning episode were associated with short-term mortality.

MATERIALS AND METHODS

Following approval by the Institutional Review Board of Virginia Mason Medical Center in Seattle, WA, patients treated for CO poisoning with hyperbaric oxygen (HBO2) therapy at the Virginia Mason Medical Center for Hyperbaric Medicine from May 1978 through December 2005 were reviewed. They were identified and basic information obtained about each through use of an institutionally approved database containing all patients treated in the facility. Additional information was extracted when necessary from the patients’ medical records available at our institution.

Although guidelines for hyperbaric treatment of CO-poisoned patients evolved over the years encompassed by this study, in general patients were accepted for HBO2 therapy if the years encompassed by this study, in general

ment of CO-poisoned patients evolved over the

from the patients' medical records available at

view Board of Virginia Mason Medical Center in

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RESULTS

A total of 1,505 patients were treated with HBO2 for acute CO poisoning from May 1978 through December 2005. Of those, 32 patients were excluded from analysis because their records contained insufficient demographic information to submit for an NDI search, leaving 1,473 patients from which the data reported were obtained. This included 961 males (65%) and 512 females (35%) ranging in age from 0 yrs to 92 yrs, and averaging 35 ± 19 yrs (mean ± SD) (median 33 yrs). The CO exposure was accidental in 1,024 patients (70%), intentional in 441 cases (30%), and indeterminate in 8 patients (1%).

NDI Plus data and records review indicated that 50 individuals (3.4%) had died within 90 days of their poisoning episode. Causes of death occurring out to 90 days after hyperbaric treatment were reviewed to ensure that all deaths directly related to the event were identified. Of them, 38 (2.6%) were consistent with being directly related to the acute poisoning event and were described as motor vehicle exhaust inhalation (12), smoke inhalation (11), fire (6), CO poisoning (6), burns (2), and intracranial hemorrhage occurring 1 day after severe poisoning (1). Deaths coded as suicide by hanging (5), suicide by motor vehicle accident (1), motor vehicle accident (1), cirrhosis (1), tongue cancer (1), drug overdose of unknown intent (1), atherosclerotic heart disease (1), and alcoholism (1) were excluded. The six suicidal deaths were not believed to be related to CO-induced mood disorders as all occurred in individuals who suffered intentional CO poisoning initially.

Of the 1,473 patients studied, 216 (15%) were treated with hyperbaric Protocol 1, 398 (27%) Protocol 2 and 859 (58%) Protocol 3 (protocol details described in Methods). Among the 38 dying from the acute poisoning episode, 8 (21%), 12 (32%), and 18 (47%) were treated with each of the protocols. Of the 38 decedents, 30 (79%) received one hyperbaric treatment and eight (21%) received two.

Individuals died 0 to 59 days following poisoning (median 2 days). Sources of CO among those who died included fires (20), motor vehicles (14), butane heater (1), furnace (1), gasoline powered electrical generator (1), and wood burning stove (1).

Demographic and clinical characteristics of the nonsurvivors and survivors are detailed in Table 1. Variables significantly different (p value <0.01) by univariate analysis between those who died and survived included fire as a source of CO, loss of consciousness, COHb level, arterial pH, and presence of endotracheal intubation during hyperbaric treatment. Subsequent stepwise logistic regression demonstrated that arterial pH (p = 0.0001) and presence of endotracheal intubation (p = 0.002) were statistically significant predictors of death. It is noted that over 40% of records were missing arterial pH measurements and were therefore excluded from analysis.
Table 1. Demographic and clinical characteristics of individuals who died of acute carbon monoxide (CO) poisoning, as compared with survivors

<table>
<thead>
<tr>
<th></th>
<th>Nonsurvivors (n = 38)</th>
<th>Survivors (n = 1435)</th>
<th>Univariate Analysis</th>
<th>Logistic Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>53% male</td>
<td>66% male</td>
<td>0.12 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Intent of poisoning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Accidental</td>
<td>70%</td>
<td>70%</td>
<td>1.0000 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Intentional</td>
<td>30%</td>
<td>30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Source of CO</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fire</td>
<td>53%</td>
<td>11%</td>
<td>&lt;0.0001 NS</td>
<td>NS</td>
</tr>
<tr>
<td>Nonfire</td>
<td>47%</td>
<td>89%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>100%</td>
<td>52%</td>
<td>&lt;0.0001 NS</td>
<td>NS</td>
</tr>
<tr>
<td>COHb%</td>
<td>31.1 ± 13.5</td>
<td>22.6 ± 12.2</td>
<td>&lt;0.0001 NS</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Initial arterial pH</td>
<td>7.20 ± 0.15</td>
<td>7.39 ± 0.10</td>
<td>&lt;0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Intubation during HBO2</td>
<td>76%</td>
<td>16%</td>
<td>&lt;0.0001</td>
<td>0.002</td>
</tr>
</tbody>
</table>

COHb, carboxyhemoglobin; HBO2, hyperbaric oxygen.

Figure 1. Initial arterial pH values vs. initial carboxyhemoglobin (COHb) levels among the 837 patients for whom both measurements were available. Equations for the linear regression lines shown are listed in the Results section.

DISCUSSION

The present study describes the largest series of patients with carbon monoxide poisoning treated with hyperbaric oxygen reported in the English literature to date and demonstrates a short-term mortality rate because of the poisoning of 2.6%. Eight other published series describing at least 100 CO-poisoned patients treated with HBO2 and reporting mortality from CO poisoning are listed in Table 2. Their combined death rate was 3.9% among 2,359 patients. Adding the present series (and subtracting the patients reported in Reference 8 because they are included herein) yields a short-term death rate of 3.1% among 3,832 patients receiving medical treatment for acute CO poisoning in large series. Because there are an estimated 50,000 emergency department visits for CO poisoning in the United States annually (1), a mortality rate of 3.1% implies approximately 1,550 deaths in the country despite hospital-based medical care.

When looking at the studies listed in Table 2, it is difficult to draw any conclusions regarding differences in mortality from CO poisoning related to the therapy administered (normobaric vs. hyperbaric oxygen). In fact, with death being such an infrequent outcome in medically treated patients, it would require a multicentered trial of enormous proportions to determine whether there is a survival advantage related to treatment.

Because of this, randomized studies to date have used neurologic sequelae as the outcome measure when examining different treatments. Neurologic sequelae are much more common than death in CO-poisoned patients. In the study by Weaver et al. (13), 18% of patients with hyperbaric oxygen manifest cognitive sequelae at 1 yr after poisoning, when compared with 33% of patients treated with normobaric oxygen. A recent expert panel report addressing unresolved issues in the treatment of CO poisoning focused on delay to treatment, number of hyperbaric treatments administered, and the specifics of the hyperbaric protocol, all with regard to neurologic outcome and not mortality (14).
It is likely that medical treatment has only a very small mortality benefit in the CO-poisoned patient. This is suggested by the fact that mortality rates are so similar across time and treatments, despite divergent patient populations (Table 2). Furthermore, some patients may experience unsurvivable insults, as was suggested in our earlier report describing 18 consecutive deaths among patients treated with hyperbaric oxygen following resuscitation from CO-related cardiac arrest (15).

Factors found by logistic regression to correlate with risk for death in the present study included arterial blood pH and presence of endotracheal intubation. In the large study by Goulon et al. (5), it was noted that mortality of CO-poisoned patients was related to the severity of metabolic acidosis. They described stepwise increases in the mortality rate as arterial pH dropped from the range greater than 7.35 to 7.35–7.25 and then to less than 7.25. Using those same categories in the present study, a similar result is seen with mortality rates of 1%, 3%, and 30% for those ranges, respectively.

Although need for endotracheal intubation and low arterial pH may simply represent severity of CO poisoning, severe systemic acidosis could be an indicator of another process. CO causes metabolic acidosis by interfering with systemic oxygen transport (COHb formation), as well as by impairing intracellular energy metabolism. It can also cause secondary impairment of oxygen delivery by reducing cardiac output because CO poisoning is known to cause myocardial injury and dysfunction (12). Figure 1 illustrates arterial pH as a function of COHb level in various subgroups of patients in this series. Regression lines drawn on Figure 1 demonstrate that the average arterial pH is lower in nonsurvivors than survivors, irregardless of CO source. One might speculate that nonsurvivors have some propensity for systemic acidosis, such as baseline anemia or cardiac dysfunction.

It should be noted that those exposed to CO from a fire source have lower arterial pH than those exposed by nonfire CO sources, both among survivors and nonsurvivors (Fig. 1). Fire was a much more common CO source among those who died. In conjunction with lower arterial pH, the possibility of concomitant cyanide poisoning should be considered. In burn victims without serious burns, elevation of plasma lactate has been shown to be a sensitive and specific indicator of cyanide intoxication (16). Unfortunately, neither cyanide nor lactate levels were present in the available records of patients in the current series. One patient who died following CO exposure from a fire was also treated for cyanide poisoning.

A recent study of patients with cyanide poisoning not associated with smoke inhalation found similar correlations between arterial pH and both blood lactate \( r = 0.87 \) and cyanide levels \( r = 0.91 \) (17). In the present study, lower pH with equivalent COHb levels among both survivors and nonsurvivors exposed to CO from fires suggests the possibility that some could have suffered from combined CO and cyanide poisoning.

The degree of elevation of the carboxyhemoglobin level is sometimes used to
Table 2. Prior publications reporting mortality rates among a minimum of 100 carbon monoxide-poisoned patients treated with hyperbaric oxygen

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Type of Treatment</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goulon et al. (5)</td>
<td>302</td>
<td>Hyperbaric oxygen 273</td>
<td>42</td>
</tr>
<tr>
<td>Mathieu et al. (6)</td>
<td>230</td>
<td>Hyperbaric oxygen 203</td>
<td>4</td>
</tr>
<tr>
<td>Myers et al. (7)</td>
<td>213</td>
<td>Hyperbaric oxygen 131</td>
<td>2</td>
</tr>
<tr>
<td>Norkool and Kirkpatrick (8)</td>
<td>115</td>
<td>Hyperbaric oxygen 115</td>
<td>11</td>
</tr>
<tr>
<td>Sloan et al. (9)</td>
<td>297</td>
<td>Hyperbaric oxygen 459</td>
<td>17</td>
</tr>
<tr>
<td>Raphael et al. (10)</td>
<td>629</td>
<td>Hyperbaric oxygen 170</td>
<td>0</td>
</tr>
<tr>
<td>Annane et al. (11)</td>
<td>343</td>
<td>Hyperbaric oxygen 170</td>
<td>0</td>
</tr>
<tr>
<td>Satran et al. (12)</td>
<td>230</td>
<td>Hyperbaric oxygen 1881</td>
<td>92 (3.9%)</td>
</tr>
<tr>
<td>Historical totals</td>
<td>2359</td>
<td>Hyperbaric oxygen 478</td>
<td></td>
</tr>
<tr>
<td>Present study</td>
<td>1473</td>
<td>Hyperbaric oxygen 1473</td>
<td>38 (2.6%)</td>
</tr>
</tbody>
</table>

The severity of CO poisoning (18). The absolute nature of such categorization has been challenged (19) and some experts feel that the correlation between clinical deficits and measured COHb level is actually quite weak (20). In the recent study by Weaver et al. (21), COHb did not correlate with 6-wk cognitive outcome. In the present study, elevation of the COHb level did correlate significantly with mortality in univariate analysis (Table 1, Fig. 2a) but extremely low arterial pH, when present, was more significantly associated with rate of death than extreme elevations of COHb level (Table 1, Fig. 2b). It is possible that COHb level and loss of consciousness were not significantly associated with death in multivariate analysis because of factors particular to each of the two variables. Time from end of CO exposure to measurement of COHb was not recorded, thereby introducing the possibility that levels in some individuals would have been much higher if obtained immediately. Similarly, loss of consciousness was recorded only as having occurred or not. Duration of loss of consciousness or depth of coma for each patient is unknown. It is possible that persistent unconsciousness correlates better with mortality than transient unconsciousness. In fact, the presence of endotracheal intubation during hyperbaric treatment may correlate strongly with death because it is a marker for more severe loss of consciousness.

Because 20 decedents in the present study were exposed to CO from fires, the possibility that burns contributed their deaths must be considered. In one large study of 1,665 burn patients, BSA involvement greater than 40% was found to be a risk factor predictive of death (22). In the present study, 1 of 8 patients had this degree of burn injury (60%). “Burns” was coded as the cause of death for only this patient and one other who had 20% BSA involvement.

To summarize, the mortality rate of CO poisoning receiving hospital-based medical treatment, including hyperbaric oxygen, is approximately 3%. Characteristics significantly associated with mortality include fire as a source of CO, loss of consciousness, carboxyhemoglobin level, arterial pH, and presence of endotracheal intubation during hyperbaric treatment. Those designing future prospective studies should consider measurement of cyanide levels in patients exposed to CO from fires to determine its contribution to metabolic acidosis as a predictor of mortality.

REFERENCES