Experience with Non-survivors of Acute Carbon Monoxide Intoxication Who Received Hyperbaric Oxygen Therapy and Literature Review

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Purpose: The main purpose of this study was to determine the reason for the carbon monoxide (CO) poisoning-related deaths at out hospital and to describe the demographic data and epidemiology.

Methods: We retrospectively selected this group of acute CO intoxication patients that received emergency hyperbaric oxygen therapy (HBOT) from April 2000 to August 2005 at our hospital. Data regarding age, gender, duration of CO poisoning exposure, cause of the episode, underlying disease, number of HBOT courses, hospital course, cormorbidity, and cause of mortality were obtained from the medical records. We also reviewed the admission data records, including vital signs, Glasgow Coma Scale, arterial blood gas, carboxyhemoglobin level, and intubation or not.

Results: One hundred thirty-seven patients and 5 fatalities related to CO poisoning were reviewed; the mortality rate was 3.65%. The 5 fatalities were all male, in the prime of life (27~37 years old), and without major underlying disease. Four (4/5) patients committed suicide by inhaling CO from burning charcoal. They all received emergent HBOT. Prolonged unconsciousness was noted after series HBOT in 4 (4/5) patients. Four (4/5) patients developed rhabdomyolysis and acute renal failure. The causes of death were multiple organ failure (3/5, 60%) and septic shock (2/5, 40%).

Conclusions: The causes of acute CO poisoning among the fatalities were suicide by inhaling CO from burning charcoal (4/5, 80%) and a fire accident (1/5, 20%) at our hospital. They were in the prime of life without major underlying disease. The brain is an oxygen-dependent organ, and the damage may be severe and irreversible after CO intoxication and hypoxia. Rhabdomyolysis and acute renal failure may also occur. Secondary infection and septic shock may worsen the already poor condition. The cause of death may be considered as multiple organ failure, including the brain, lung, and kidney. ***(Thorac Med 2008; 23: 187-194)***

Key words: acute carbon monoxide poisoning, hyperbaric oxygen therapy, mortality cases, multiple organ failure

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Introduction

Carbon monoxide (CO) is a product of the incomplete combustion of hydrocarbons. CO is a colorless, odorless, and nonirritant toxic gas that is easily absorbed through the lung. Its production does not have a special warning sign. As many as 3,500 people are poisoned and die in the United Sates (US) every year because of CO poisoning related to fire, coal gas, automobile exhaust, and other sources [1]. The amount of gas absorbed is dependent on the minute ventilation, the duration of exposure, and the relative concentration of CO and oxygen in the environment [2]. CO toxicity appears to result from a combination of tissue hypoxia and direct CO-mediated damage at the cellular level [3]. Hyperbaric-oxygen therapy (HBOT) is often recommended for patients with acute CO poisoning, especially if they have lost consciousness or have severe poisoning [4]. The advantages of HBOT include increased dissolved-oxygen content in the blood and accelerated elimination of CO [5]. The potential benefits of HBOT include the prevention of lipid peroxidation in the brain and the preservation of adenosine triphosphate (ATP) levels in tissue exposed to CO [5].

We selected a group of acute CO intoxication patients that had received emergency HBOT from April 2000 to August 2005. The main purpose of this study was to determine the reason for the CO-related deaths and to describe the demographic data and epidemiology of these fatal poisonings.

Materials and Methods

The Hyperbaric Oxygen Therapy Center of China Medical University Hospital (CMUH), Taichung, Taiwan was established in April 2000. We use a multiplace hyperbaric chamber (HPE. 50.2M Model 222.12.AT, Bergamo, Italy).

We retrospectively reviewed the records of the patients who received HBOT at CMUH from April 2000 to August 2005 due to acute CO poisoning. During the 5-year study period, 137 patients who received HBOT for acute CO poisoning were enrolled, and 5 CO poisoning-related deaths are described. Data on the age, gender, duration of CO poisoning exposure, cause of the episode, underlying disease, number of HBOT courses, hospital course, cormorbidity, and cause of mortality were obtained from the medical records. We also reviewed the admission data records, including vital signs, Glasgow Coma Scale (GCS), arterial blood gas, carboxyhemoglobin (HbCO) level, and intubation or not.

Results

The records of 137 patients were reviewed. Seventy-four (73/137, 53%) patients were women, and 64 (64/137, 47%) were men. Eighteen (18/137, 13%) patients had been intubated with mechanical ventilator support due to acute respiratory failure. The causes of CO poisoning included attempted suicide by inhaling CO from burning charcoal (71%, 97/137), bathing accidents with gas inhalation (20%, 27/137), fire accidents (3%, 5/137), attempted suicide by inhaling automobile exhaust (3%, 4/137), barbecue accidents with coal gas inhalation (2%, 3/137), and a work accident with other toxic gas inhalation (1%, 1/137). Twenty-five (25/137, 18%) patients were abusing sedative drugs when they attempted suicide with CO poisoning.

Five patients died due to CO poisoning, with

a mortality rate of 3.65%. All were males, in the prime of life (27~37 years old), and without major underlying disease. They were sent to our Emergency Department (ED) due to attempted suicide through inhaling CO fumes from burning charcoal (4/5, 80%) and a fire accident (1/5, 20%). The duration of exposure to CO could not be clearly ascertained. The level of HbCO ranged from 11.4% to 56.9%. The patients were in a deep coma when they arrived at our ED. Two (2/5) patients were dead on arrival (DOA) and were resuscitated from cardiac arrest; 3 (3/5) were intubated with mechanical ventilator support, and 2 (2/5) used 100% oxygen initially. The patients were treated in the multiplace hyperbaric chamber (HPE.50.2M Model 222.12.AT, Bergamo, Italy), under 2.5 atmospheric pressure absolute (ATA), with 100% oxygen for 23 minutes and an air break for 5 minutes, with the duration averaging 2 hours (1.5~3 hours), and 1~3 times per day. Prolonged unconsciousness was noted after series HBOT in these patients. Three (3/5) patients developed rhabdomyolysis due to extended tissue compression, and 4 (4/5) developed acute renal failure. The length of hospitalization was from 2 to 18 days. Table 1 summarizes the data presented in this study. The causes of death were multiple organ failure (3/5, 60%) and septic shock (2/5, 40%).

Discussion

In Taiwan, suicide has been the 9th leading cause of death in recent years, and CO poisoning is the number 2 cause of successful suicide. CO poisoning accounts for an estimated 40,000 annual ED visits in the US; it is the leading cause of poisoning mortality in the US and may be responsible for more than half of all fatal poisonings worldwide [3]. CO is the commonest and most serious by-product of combustion, and is responsible for smoke-related morbidity and mortality [6]. As it is a colorless, odorless, tasteless and non-irritating gas, the exposed person is usually unaware of its effect until serious disorders occur. CO causes poisoning by its high affinity to hemoglobin (200 to 250 times greater than its affinity for oxygen) and its ability to replace oxygen, which renders the hemoglobin useless in terms of its oxygen carrying capacity. CO also alters the molecular configuration of hemoglobin and decreases the 2-3 diphosphoglycerate (2-3 DPG) of red blood cells, resulting in an unfavorable left shift of the oxyhemoglobin dissociation curve [7]. These alterations result in an impaired release of oxygen at the tissue level, and cellular hypoxia.

The amount of gas absorbed is dependent on the minute ventilation, the duration of exposure, and the relative concentrations of CO and oxygen in the environment. CO is principally eliminated by the lungs as an unchanged gas. CO binds to many heme-containing proteins other than hemoglobin, including cytochromes, myoglobin, and guanylyl cyclase. The disruption of oxidative metabolism via cytochrome oxidase may lead to the generation of oxygen free radicals. Cellular respiration may also be impaired via inactivation of mitochondrial enzymes and impaired electron transport from oxygen radicals (i.e., peroxynitrite) produced after CO exposure [8]. Clinical manifestations of CO intoxication are related to the blood carboxyhemoglobin level, time course of exposure, respiratory rate, age and health of the victim, and concomitant medications (affecting hepatic enzymes) or toxins (drugs, alcohol, etc.) [9]. The duration of exposure appears to be an important factor mediating toxicity. The CO

Table 1. Patient data

No.	Age (y)	Sex	Cause on Arrival	HbCO (%)	G.C.S. on arrival	ET	HBOT Number	Days of Admission	Cormorbidity	Underlying Disease	Cause of Death
1	35	M	Charcoal burning	37.6	E1VEM1	Y	1	2	1. Right leg compartment syndrome S/P fasciotomy 2. Rhabdomyolysis with acute renal failure S/P emergent hemodialysis 3. Aspiration pneumonia	1. Depression 2. Insomnia	CO intoxication with hypoxic encephalopathy and multiple organ failure
2	33	M	Charcoal burning	46.2	E1V1M2	N	2	18	1. Aspiration pneumonia 2. K.P. bacteremia	Major depression	Meningitis with septic shock
3	37	M	Charcoal burning	56.9	E1VEM1	Y	1	2	1. Acute renal failure	Nil	CO intoxication with hypoxic encephalopathy and multiple organ failure
4	27	M	Fire accident	33.2	E1VEM1	Y	1	6	1. Rhabdomyolysis with acute renal failure 2. Refractory seizure	Nil	CO intoxication with hypoxic encephalopathy and multiple organ failure
5	29	M	Charcoal burning	11.4	E4V5M6	N	1	10	1. Rhabdomyolysis with acute renal failure 2. Necrotizing fascitis	1. Mood disorder	Septic shock with multiple organ failure

No.=number; y=years old; ET=intubation; M=male; Y=yes; N=no; K.P.=Klebsiella Pneumoniae; CPCR=cardiopulmonary and cerebral resuscitation; HbCO=carboxyhemoglobin; D.O.A.=dead on arrival; G.C.S.=Glasgow Coma Scale

level is certainly important in diagnosing CO poisoning, but does not predict the immediate or late sequelae. The decision to administer HBOT or not cannot be made solely on the basis of CO levels [10]. By supplying a high concentration of oxygen or HBOT (100 percent oxygen at 2 to 3 times the atmospheric pressure at sea level) in victims of CO poisoning, CO can be replaced by oxygen and tissue hypoxia can be relieved. The half-life of CO in the body is approximately 4-5 hours; this can be reduced to 60-80 minutes by giving 100% oxygen, or to approximately 25 minutes by HBO [3]. HBOT with CO-poisoned individuals is more effective when delivered within 6 hours of removal from CO exposure [11].

Acute CO poisoning is a common event with variable presentations. The symptoms and signs are distributed from headache, dizziness, weakness, nausea, shortness of breath, visual changes, chest pain, difficulty concentrating, and confusion, to loss of consciousness. The clinical effects of CO poisoning are diverse and easily confused with other illnesses, such as nonspecific viral illnesses, benign headache, and various cardiovascular and neurological syndromes [3]. Early neurological manifestations include dizziness and headache. Increasing exposure may produce altered mental status, confusion, syncope, seizure, acute stroke-like syndromes, and coma.

The role of nitric oxide (NO) and other oxygen free radicals has been researched extensively in the setting of CO poisoning. Many animal studies have demonstrated cerebral vasodilation after exposure to CO, which is associated temporally with a loss of consciousness and increased NO levels. This finding has led to speculation that clinical syncope may be related to NO-mediated cerebral vessel relaxation and low blood flow. NO is also a peripheral vasodilator and may result in systemic hypotension [5]. The presence of systemic hypotension in CO poisoning is correlated with the severity of central nervous system structural damage [12]. NO also seems to play a pivotal role in a cascade of events culminating in oxidative damage to the brain, which may be responsible for the clinical syndrome of delayed neurological sequelae (DNS). Brain lipid peroxidation after CO exposure seems to be a post-ischemic reperfusion phenomenon, mediated by alterations in cerebral blood flow and oxidative free radical damage [8].

Due to coma consciousness secondary to CO poisoning, long-term muscle compression and hypoxic encephalopathy with refractory seizure may result in rhabdomyolysis, cell lyses with hyperkalemia, metabolic acidosis, acute tubular necrosis, oliguria, and acute renal failure. CO poisoning may also result in rhabdomyolysis, potentially as a direct toxic effect of CO on skeletal muscles [13].

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%, and are estimated to average 20% overall. Discovery of the arrested patient in asystole or bradydysrhythmia has also been described as associated with a worse prognosis [14]. It can be seen that cardiac arrest complicating CO poisoning carries a dismal prognosis, even if resuscitation yields a return of spontaneous circulation and the patient subsequently undergoes HBOT. Neil and Jennette found that cardiac arrest complicating CO poisoning resulted in 100% mortality, despite initial resuscitation in the field with a return of spontaneous circulation and subsequent HBOT

[15].

Case number 4 (Table 1) was poisoned by CO in a house fire. He might have had concomitant poisoning with other toxins, particularly cyanide. In an Australian study, many of the victims died with elevated whole blood cyanide levels, which are significantly correlated with HbCO levels. Further research is required to determine the frequency of toxic cyanide levels in smoke inhalation patients who are transported to the hospital [22]. This was documented in a report of patients undergoing cardiac arrest sustaining CO poisoning from smoke inhalation [23].

In our review of the 5 mortality cases, all patients were healthy and in the prime of life. When they arrived at our ER, an unstable hemodynamic status, deep coma, and acidosis (mixed respiratory and metabolic acidosis) were noted. The brain is the most oxygen-dependent organ and the most sensitive to the toxic effects of CO [3]. Four (4/5, 80%) of the 5 mortalities were persistently comatose; we believe that the damage to the brain was severe and irreversible. Rhabdomyolysis, hyperkalemia, and acute renal failure may occur due to muscle compression, but the course of death is mostly due to multiple organ failure (brain, respiratory, and renal failure).

On the basis of this experience and a review of the available literature, long-term exposure, severe CO poisoning, and multiple organ failure may considered as poor prognostic factors for survival. There are currently no standard recommendations regarding the factors leading to a poor prognosis or the use of HBOT in these patients. Further research is needed to define these factors and help in the decision to institute active cardiopulmonary resuscitation or treatment.

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急性一氧化碳中毒病人接受高壓氧治療後死亡病例臨床經驗分析和文獻回顧

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目的：針對急性一氧化碳中毒患者死亡者分析其治療經過及探討其死亡原因。

方法：我們回溯性研究近5年來(從2000年4月至2005年8月)，因為急性一氧化碳中毒送到中國醫藥大學附設醫院，接受高壓氧治療的患者。我們從病歷中收集病人的性別、年齡、中毒原因、一氧化碳中毒時間、高壓氧治療次數、住院時間、併發症、治療經過、以及死亡原因等，並紀錄到院時生命徵象、昏迷指數、一氧化碳濃度、血氧分析、以及有無氣管插管等相關資料。

結果：我們總共收治了137例一氧化碳中毒的患者，其中五例死亡，死亡率為3.65%。五例死亡患者中男性五例，女性零例，年齡27~37歲，正處於青壯年，且無重大疾病;四例為燃煤自殺；一例為火災意外。病人由急診會診後立即進行高壓氧治療。其中四例直到死亡前意識仍無法恢復；四例發生橫紋肌溶解症和急性腎衰竭。死亡原因分別為多重器官衰竭（三例）和敗血性休克（二例）。

結論：本院死亡病例以自殺為主(80%)，且均為青壯年。腦是一個需氧且對缺氧很敏感的器官，在一氧化碳中毒及缺氧後所造成傷害或許是嚴重且不可逆的。橫紋肌溶解症併急性腎衰竭、次發性感染、和敗血性休克或許會使情況更加惡化。但最後死亡原因應該仍為多重器官衰竭，包括了腦、肺、和腎臟。
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關鍵詞：急性一氧化碳中毒，高壓氧治療，死亡病例，多重器官衰竭

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