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Full Length Research Paper

Clinical manifestation, effects, diagnosis, monitoring of carbon monoxide poisoning and toxicity

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Carbon monoxide is a product of incomplete combustion of organic matter with insufficient oxygen supply to enable complete oxidation to carbon dioxide (CO_2) and is often produced in domestic or industrial settings. In this study the clinical manifestation, effects, diagnosis and toxicity of carbon monoxide poisoning were reviewed. Research suggests that the intracellular uptake of carbon monoxide is an important mechanism for neurologic damage. As a result upon the review of many articles and research journals, it is identified that carbon monoxide may be quantitated in blood using spectrophotometric methods or chromatographic techniques in order to confirm the diagnosis of poisoning in hospitalized victims or to assist in the forensic investigation of a case of fatal exposure. A brain computed tomography (CT) scan may be normal in early stages or show signs of cerebral edema. Public education on the safe operation of appliances, heaters, fireplaces and internal combustion engines is required for prevention of CO poisoning. Carbon monoxide detectors with alarms can improve home safety and their use is recommended by various safety organizations.

Key words: Carbon monoxide, toxicity, hemoglobin.

INTRODUCTION

Carbon monoxide has been unknowingly used by humans since prehistoric times, for the smelting of iron and other metallic ores. The gas was used for executions by the Greek and Romans in “classical antiquity”, and was first described by the Spanish doctor Arnaldus de Villa Nova in the 11th century. In 1776, the French chemist de Lassone produced CO by heating zinc oxide with coke (fuel), but mistakenly concluded that the gaseous product was hydrogen as it burned with a blue flame. The gas was identified as a compound containing carbon and oxygen by the Scottish chemist William Cumberland Cruikshank in the year 1800. Its toxic properties on dogs were thoroughly investigated by Claude Bernard around 1846 (Cobb and Etzl, 1991).

SOURCES OF CARBON MONOXIDE

The human body produces carbon monoxide as a by product of hemoglobin degradation, resulting in baseline carboxyhemoglobin (COHb) saturation of 1 to 3% in non-smokers and 10 to 15% amongst heavy smokers. A smoker is exposed to 400 to 500 ppm of CO while actively smoking (Cobb and Etzl, 1991). According to ten years review of carbon monoxide related deaths, more than half of unintentional deaths were caused by motor vehicle exhaust (Cobb and Etzl, 1991). Burning of charcoal, wood, kerosene, or natural gas for heating and cooking also produces carbon monoxide (Raub et al., 2000). In army setting, poisoning is usually seen in high-altitude areas where unwary soldiers often sleep in closed tents with burning bhukharis (charcoal/kerosene) kept inside (Grace and Platt, 1981). Carbon monoxide can occur in the presence of other factors, complicating its management. It is a major contributor in thousands of smoke inhalation deaths that occur each year.

People, who work with methylene chloride as paint stripper, can be poisoned because the fumes are readily absorbed and converted to CO in the liver (Meredith and Vale, 1988). In such cases, peak COHb levels may be delayed and prolonged because of on going production of CO from liver.

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TOXICITY OF CO

The amount of CO absorbed by the body depends on minute ventilation, duration of exposure and concentration of CO in the environment. Carbon monoxide quickly binds with hemoglobin with an affinity greater than that of oxygen to form COHb. The resulting decrease in arterial oxygen content and shift of the oxyhemoglobin dissociation curve to the left explains the acute hypoxic symptoms (primarily neurologic and cardiac) seen in patients with acute poisoning (Mehta et al., 2001). But the toxic effects of CO cannot be explained by these processes alone, as COHb levels do not correlate well with symptoms, outcomes or the phenomenon of delayed neurologic sequelae (Ely et al., 1995). Research suggests that the intracellular uptake of carbon monoxide is an important mechanism for neurologic damage. When carbon monoxide binds to cytochrome oxidase, it causes mitochondrial dysfunction resulting into oxidative stress related damage (Prockop and Chichkova, 2007). The release of nitric oxide from platelets and endothelial cells, which forms the free radical peroxynitrite, can further inactivate mitochondrial enzymes and damage the vascular endothelium of the brain (Myers and Synder, 1985). The end result is lipid peroxidation of the brain, which starts during recovery from carbon monoxide poisoning. With reperfusion of the brain, leukocyte adhesion and the subsequent release of destructive enzymes and excitatory amino acids all amplify the initial oxidative injury (Burney, 1982). The net result is cognitive defects, particularly in memory and learning with movement disorders that may not appear for days following the initial poisoning.

Carbon monoxide exposure has an especially deleterious effect on pregnant women, because of the greater sensitivity of the foetus to the harmful effects of the gas. The final COHb levels in the foetus significantly exceed the level of the mother (Remick and Miles, 1997). The excessive left shift of foetal COHb curve makes tissue hypoxia more severe by releasing less oxygen to the foetal tissues (Sato et al., 1990). Although the teratogenicity of CO is controversial, the risk of foetal injury is increased (Remick and Miles, 1997; Sato et al., 1990). Once CO exposure is discontinued, dissociation of COHb occurs and CO is excreted through the lungs. At atmospheric pressure, the COHb half-life is 4 to 6 h which decreases to 40 to 80 min on breathing 100% oxygen.

Effects of CO

Patients can successfully recover from acute CO poisoning only to return, days later with serious neurological problems, ranging from subtle cognitive deficits (apparent on neuropsychological testing) to gross incapacitating movement disorders, resulting from carbon monoxide's predilection for basal ganglia (Tibbles, 1996). Within a day of high CO exposure, neuroimaging can show decreased density in the central white matter and globus pallidus. Autopsies have shown involvement of cerebral cortex, hippocampus, cerebellum, and substantia nigra. Neurologic sequelae may be evident immediately or may occur after a lucid interval of up to three weeks. The incidence of such sequelae can be as high as 40% (for memory impairment), and they may persist for more than a year. Children may present with behavioral or learning problems, while the elderly appear to be more susceptible to devastating consequences (Burney, 1982; Sato et al., 1990).

The development of neurologic sequelae cannot be reliably predicted. However, most cases are associated with loss of consciousness in the acute phase of intoxication (Hark and Kennedy, 1998). The standard CO neuropsychological screen battery helps in objective evaluation of such patients.

Severe CO poisoning

The symptoms of low level chronic CO intoxication are non-specific, and unlikely to arouse suspicion of CO as the cause. It can also exacerbate the preexisting diseases like ischaemic heart disease or dementia (Sato et al., 1990). Patients present with bizarre behavioural abnormalities declining intellect, memory disturbances, chronic cough or diarrhoea. The condition is often misdiagnosed as chronic fatigue syndrome, a viral, bacterial, pulmonary, gastrointestinal infection or immune deficiency. Patients may occasionally present with polycythemia or increased hematocrit. COHb is usually not excessively elevated.

Clinical manifestations

Clinical manifestations of acute CO poisoning can be vague and may closely mimic various nonspecific viral illnesses. CO poisoning usually affects many people at the same time. The acute symptoms of CO poisoning are reflected in the susceptibility of the brain and heart. Initially, patients may complain of headache, dizziness, nausea, emotional liability, confusion, impaired judgment, clumsiness and syncope (Ely et al., 1995; Myers and Synder, 1985; Burney, 1982). Vomiting may be the only presenting symptom in infants and may be misdiagnosed as gastroenteritis. Coma or seizures can occur in patients with prolonged CO exposure (Hark and Kennedy, 1998). Elderly patients, especially those with coronary artery disease, may have accompanying myocardial ischaemia, which may result in frank myocardial infarction (Sato et al., 1990). Prolonged exposures resulting in coma or altered mental status may be accompanied by retinal hemorrhages and lactic acidosis (Ely et al., 1995).

Myonecrosis can occur but it rarely leads to compartment syndrome or renal failure. Cherry-red skin color associated with severe carbon monoxide

Table 1. Comparison of clinical features between Mehta et al and Pooled data Ely et al.

Clinical features	Mehta et al. (n = 25)% of patient	Pooled data (Ely et al., Myers et al., and Burney) (n = 196)% of patient
Drowsiness and/ or confusion	48	43
Coma	24	6
Hemiparesis	24	6
Seizures	12	-
Angina pectoris	8	9
Dyspnoea/ tachypnoea	80	40
Tachycardia	64	-
Cherry red skin	24	-

Table 2. Levels of COHb and clinical manifestations

Concentration (%)	Symptoms
35 ppm (0.0035)	Headache and dizziness within six to eight hours of constant exposure.
100 ppm (0.01)	Slight headache in two to 3 h.
200 ppm (0.02)	Slight headache within two to three hours; loss of judgment.
400 ppm (0.04)	Frontal headache within one to 2 h.
800 ppm (0.08)	Dizziness, nausea, and convulsions within 45 min; insensible within 2 h.
1,600 ppm (0.16)	Headache, tachycardia, dizziness, and nausea within 20 min; death in less than 2 h.
3,200 ppm (0.32)	Headache, dizziness and nausea in five to ten minutes. Death within 30 min.
6,400 ppm (0.64)	Headache and dizziness in one to two minutes. Convulsions, respiratory arrest, and death in less than 20 min.
12,800 ppm (1.28)	Unconsciousness after 2 to 3 breaths. Death in less than 3 min.

poisoning is seen in only 2 to 3% of symptomatic cases (Burney, 1982). Various clinical features for evaluation of such cases are shown in Table 1.

Skin may develop erythematous lesions and bullae especially over bony prominences. Severe poisoning often leads to hypotension and pulmonary edema with the former is the most reliable marker of overall prognosis. The acute effects produced by carbon monoxide in relation to ambient concentration in parts per million are listed in Table 2.

Diagnosis

Physicians should be alert for the symptoms of carbon monoxide poisoning, especially during the winter, when risk of continued prolonged exposures may be greater. Patients who present with flu-like symptoms (that is headache, nausea, and dizziness) should be questioned about the use of gas or oil based heating appliances at home or work. The same symptoms occurring in housemates are also a warning sign of environmental exposure. Criteria for admission and prolonged observation of such cases are shown in Table 3. A hand held breath analyzer can be used to quickly rule out carbon monoxide poisoning. However, the incidental presence of ethanol can result in a false-positive reading. Comatose patients can be monitored for rhabdomyolysis by measuring creatine kinase (CK) levels. A brain computed tomography (CT) scan may be normal in early stages or show signs of cerebral oedema. Subsequently CT may show symmetrical bilateral hypodensities of the basal ganglia, particularly of the globus pallidus and substantia nigra. The other abnormalities may be subcortical white matter hypodensities, cerebral cortical lesions, hippocampal lesions, and loss of gray-white differentiation.

The electro encephalogram usually demonstrates diffuse slowing which is of little prognostic value. Single photon emission computed tomography (SPECT) has also been used in CO poisoning cases.

Detection in biological specimens

Carbon monoxide may be quantitated in blood using spectrophotometric methods or chromatographic techni-ques. This is done in order to confirm a diagnosis of poisoning in hospitalized victims or to assist in the forensic investigation of a case of fatal exposure.

Carboxyhemoglobin blood saturations may range up to 8 to 10% in heavy smokers or persons extensively exposed to automotive exhaust gases. In symptomatic poisoned patients they are often in the 10 to 30% range, while persons who succumb may have postmortem blood levels of 30 to 90% (Sato et al., 1990).

Table 3. Criteria for admission and prolonged observation.

1.	Loss of consciousness.
2.	Neurological deficit at any time.
3.	Clinical or electrocardiographic signs of cardiac compromise.
4.	Metabolic acidosis.
5.	Abnormal chest radiograph.
6.	COHb level >25%,COHb level >15% with a history of cardiac disease or > 10% in a pregnant patient.
7.	PO<60 mm Hg.

Table 4. Indications for HBO therapy in CO poisoning.

1.	Comatose patients.
2.	Any period of unconsciousness.
3.	Any abnormal score on the Carbon monoxide neuropsychological screening battery.
4.	Patients with COHb levels >40%.
5.	Cardiovascular involvement (chest pain, ECG changes arrhythmias).
6.	History of ischaemic heart disease and COHb levels >15%.
7.	Pregnant patients with COHb levels >15%.
8.	Patients who do not respond to 100% oxygen after 4 to 6 h.
9.	Patients with recurrent symptoms up to three weeks after exposure.

TREATMENT

The initial treatment of patients with symptomatic carbon monoxide poisoning is relatively straightforward. Non-re-breather mask supplies 100% oxygen to quickly clear COHb from the blood and this therapy reduces the half-life of COHb from about 4 to 5 h to 1 h (Grace and Platt, 1981). Oxygenation at a peripheral setup can be given with a simple oro-nasal plastic mask at a flow rate of 6 to 10 litres/minute which gives oxygen concentration of about 35 to 50%. Oxygen delivery with face mask with reservoir corticosteroids, mannitol, hypothermia and hyperventilation has been recommended in serious cases of CO poisoning but their benefit has not been proved.

HBO therapy

Hyperbaric oxygen therapy (HBO) for the treatment of carbon monoxide (CO) poisoning was first discussed by Haldane in the 1890s and was first used in the 1960s (Smith, 1962). At the time, CO toxicity was thought to result entirely from the relative anemia and hypoxia imposed by the formation of carboxyhemoglobin (CO-Hgb) (Haldane, 1972). We now know that the pathophysiology of CO poisoning is much more complex and involves direct toxicity at the cellular level (Kao and Nanagas, 2005). Mechanisms and potential treatments for CO poisoning are an area of active basic science and animal research. Clinically intriguing is a syndrome of apparent recovery followed approximately 2 weeks later by behavioral and/or neurologic deterioration. This is known as delayed neurologic sequelae (DNS) and it may be debilitating and permanent (Thom and Keim, 1989; Min, 1983; Myers et al., 1985; Prockop; 2005). The exact cause and incidence of DNS remains elusive as does of a precise definition. Indications for HBO therapy in CO poisoning is given in Table 4.

Chem-optical (gel cell) technology

Chem-optical technology (or gel cell or biomimetic technology) alarms use a type of sensor that simulates haemoglobin in the blood.

Electrochemical alarm

Electrochemical alarms work by converting the carbon monoxide electrochemically to carbon dioxide, which generates an electrical current that is taken as a measure of the gas concentration. Electrochemical alarms are usually powered by a battery lasting about five years.

Semiconductor technology

These alarms use semiconductors or tin dioxide technology to detect carbon monoxide levels. Unlike the alarms above, semiconductor detector alarms do not

require any replacement sensors. The British Standards Institute (BSI) is a national standards body, responsible for ensuring products meet certain agreed standards of safety. BSI standard BS7860 is the one for monitors that detect carbon monoxide at levels well before they become dangerous for humans (Tibbles, 1996). Prevention requires public education on the safe operation of appliances, heaters, fireplaces and internal combustion engines. Increased awareness amongst soldiers posted to cold/high altitude areas about the dangers of using sigris and bhukharis in enclosed places like tents/bashas/barracks/rooms will go a long way in preventing CO poisoning and deaths.

Burned victims, with evidence of smoke inhalation from an enclosed fire, should undergo testing for COHb levels. During winters, CO poisoning should be suspected in patients presenting with flu-like symptoms (for example headache, dizziness and nausea), which they may not attribute to a faulty furnace or other heating sources. Carbon monoxide detectors with alarms can improve home safety and their use is recommended by various safety organizations.

PREVENTION

Carbon monoxide detectors are available from most local hardware. They can provide an audible high-pitched alarm when high levels of carbon monoxide are detected or provide an alarm plus a digital display of the concentration of carbon monoxide detected in units of 'parts per million' (ppm). Three types of carbon monoxide detectors are available.

CONCLUSIONS

Carbon monoxide poisoning is a multi-system condition and can cause a confusing constellation of clinical features, precipitating presentation to general practitioners, accident and emergency departments, acute care physicians, general surgeons, neurologists and even psychiatrists. With increasing specialization within the medical profession the diagnosis may be missed by the specialist who fails to recognize the significance of pathology outside his or her own area of interest. The benefits of prompt diagnosis are threefold. Firstly, recommended therapy, in the form of 100% normobaric oxygen in all cases and hyperbaric oxygen in cases of life threatening poisoning can be instigated.

Secondly, as illustrated by this case, unnecessary expensive and painful investigations can be avoided. Thirdly, and perhaps most importantly, the dire consequences of discharging a patient home to, or allowing others access to a potentially fatal environment can be avoided.

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