Carbon Monoxide Poisoning

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Introduction

Carbon monoxide (CO) is a nonirritating colourless, odourless gas produced by incomplete burning of carbon containing fossil fuels. The normal concentration in atmosphere is less than 0.001% and a concentration of 0.1% can be lethal. It causes thousands of uncalled for deaths each year. Patients who survive the initial poisoning can develop delayed neurologic dysfunction, which occurs in 14-40% of serious cases. At present CO is one of the commonly encountered poison in our environment and a leading cause of poisoning world wide [1-3]. Poisoning can be acute, subacute and chronic [4].

Sources of Carbon Monoxide

The human body produces carbon monoxide as a byproduct of hemoglobin degradation, resulting in baseline carboxyhemoglobin (COHb) saturation of 1-3% in non-smokers, which increases to 10-15% amongst heavy smokers. A smoker is exposed to 400 to 500 ppm of CO while actively smoking [1,2]. According to a ten year review of carbon monoxide related deaths more than half of unintentional deaths were caused by motor vehicle exhaust [1]. Burning of charcoal, wood, kerosene, or natural gas for heating and cooking also produces carbon monoxide [5]. 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 [6].

Carbon monoxide can occur in the presence of other toxins, complicating management. It is a major contributor in the thousands of smoke inhalation deaths that occur each year [1]. 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 [4]. In such cases, peak COHb levels may be delayed and prolonged because of on going production of CO from liver.

Toxicity

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 [5]. But the toxic effects of CO cannot be explained by these processes alone, as COHb levels do not correlate well with symptoms, outcome or the phenomenon of delayed neurologic sequelae [2,7].

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 [8]. 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 [9]. 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 [10-12]. 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 exceeds the level in the mother [13]. The excessive left shift of foetal COHb curve makes tissue hypoxia more severe by

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releasing less oxygen to the foetal tissues [14]. Although the teratogenicity of CO is controversial, the risk of foetal injury is increased [15-17]. Once CO exposure is discontinued, dissociation of COHb occurs and CO is excreted through the lungs. At atmospheric pressure, the COHb half-life is four to six hours which decreases to 40-80 minutes on breathing 100% oxygen.

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 to hypoxia. Initially, patients may complain of headache, dizziness, nausea, emotional lability, confusion, impaired judgment, clumsiness and syncope [7, 18,19]. 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 [2]. Elderly patients, especially those with coronary artery disease, may have accompanying myocardial ischaemia, which may result in frank myocardial infarction [12]. The clinical manifestations are depicted in Table 1.

Prolonged exposures resulting in coma or altered mental status, may be accompanied by retinal hemorrhages and lactic acidosis [7]. Myonecrosis can occur but it rarely leads to compartment syndrome or renal failure. Cherry-red skin colour associated with severe carbon monoxide poisoning, is seen in only 2-3% of symptomatic cases [13]. Skin may develop erythematous lesions and bulla especially over bony prominences. Severe poisoning often leads to hypotension and pulmonary oedema with the former being the most reliable marker of overall prognosis. The clinical features are depicted in Table 2.

Persistent and Delayed Effects

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 [14]. 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 behavioural or learning problems, while the elderly appear to be more susceptible to devastating consequences [20,21]. The development of neurologic sequelae cannot be reliably predicted, however, most cases are associated with loss of consciousness in the acute phase of intoxication [2]. The standard CO neuropsychological screen battery helps in objective evaluation of such patients.

Chronic 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 [22]. 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.

Table 1
Levels of COHb and clinical manifestations

Blood COHb concentration (%)	Clinical manifestations
15-20	Mild headache, easy fatigability
20-30	Pounding headache, impaired motor dexterity, blurring of vision, irritability
30-40	Severe muscle weakness, nausea, vomiting, mental confusion or delirium
40-50	Tachycardia, cardiac irritability
50-60	Seizures, respiratory insufficiency
> 60-70	Coma, respiratory failure, death

Table 2

Method	Advantages	Disadvantages
Spectrophotometric analysis	Quantitative assessment Rapid Guide for therapy	Delay in analysis may lead to spuriously normal COHb levels Costly and not readily available
Kunkel's test (5 to 6 drops of 3% tannic acid added to patient's diluted blood gives a persistent crimson red coagulum)	Rapid field test	Only qualitative analysis
Pulse oxymetry	Non invasive bed side test	Unreliable because it grossly over estimates oxygen saturation in the presence of COHb
Arterial blood	Useful to confirm lactic acidosis, which is a marker of prolonged, serious exposure to carbon monoxide	Measures dissolved oxygen and thus overestimates the true oxygen saturation of hemoglobin

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 (i.e., headache, nausea, 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. Various clinical features for evaluation 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. Later on 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 electroencephalogram usually demonstrates diffuse slowing which is of little prognostic value. Single photon emission computed tomography (SPECT) has also been used in CO poisoning cases.

Treatment

The initial treatment of patients with symptomatic carbon monoxide poisoning is relatively straightforward. A 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 4-5 hours to one hour [4]. 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 35-50%. Oxygen delivery with face mask with reservoir

bag and a flow rate of 8-10 litres/ minute provides an oxygen concentration of about 70-80%. Face mask with reservoir bag and directional valve with flow rate of 10-15 litres/ minute achieves oxygen concentration of about 90-95%. Hypotension is treated with fluids and vasopressors. In confused patients, a finger stick glucose test is essential to rule out hypoglycemia. Occasional seizure may require administration of benzodiazepines. Patients with suspected coronary artery disease may benefit from an electrocardiogram, CK testing, and therapy for angina. Kidneys can be protected from rhabdomyolysis with aggressive hydration to increase urination. The criteria for intensive care admission are shown in Table 4.

Hyperbaric Oxygen Therapy

Hyperbaric oxygen therapy (HBO) involves enclosing the patient in a pressure chamber and administering 100% oxygen at a pressure greater than 1 atmosphere absolute (ATA). HBO at 2.5 ATA reduces the half-life of COHb to about 20 minutes. HBO has been used in CO poisoning management since 1962 [22]. In addition to accelerated rate of CO elimination from hemoglobin, removal from intracellular binding sites is also enhanced by HBO treatment. The timely administration of HBO prevents neuronal injury, prevents delayed neuropsychological sequelae and terminates the biochemical deterioration. [21-23]. Suggested indications for HBO therapy in CO poisoning are given in Table 5. Adjunctive therapy such as administration of

Table 3

Clinical features	Mehta et al [6] (n=25)% of patient	Pooled data Ely et al[7], Myers et al [18] and Burney [19] (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 4

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. $PO_2 < 60$ mm Hg

Table 5

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 4-6 hours
9. Patients with recurrent symptoms up to three weeks after exposure

corticosteroids, mannitol, hypothermia and hyperventilation has been recommended in serious cases of CO poisoning but their benefit has not been proved.

Prevention

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. Burn 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 (e.g., headache, dizziness, 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 [24-26].

Conflicts of Interest

None identified

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