Review Article

Carbon Monoxide Poisoning

Surg Cdr Kamal Mishra[a], Surg Capt Gokul Krishnan[b]

Abstract

Introduction : Carbon monoxide is known as the silent killer, being colorless, odourless, and tasteless. Initially non-irritating, it is very difficult for people to detect. Carbon monoxide is a product of incomplete combustion of organic matter due to insufficient oxygen supply that prevents complete oxidation of carbon to CO2.

During World War II, Nazis used gas vans to kill an estimated over 700,000 prisoners by carbon monoxide poisoning. This method was also used in the gas chambers of several death camps. The true number of incidents of carbon monoxide poisoning is unknown, since many non-lethal exposures go undetected. From the available data, carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide.

Clinical features and management : The signs of carbon monoxide poisoning vary with concentration and length of exposure. Subtle cardiovascular or neurobehavioural effects occur at low concentration. The onset of chronic poisoning is usually insidious and easily mistaken for viral prodrome, depression, or gastroenteritis in children. The classic sign of carbon monoxide poisoning which is actually more often seen in the dead than the living is appearing red-cheeked and healthy. Cherry pink colour develops in nails, skin and mucosa. In acute poisoning, common abnormalities of posture and tone are cogwheel rigidity, opisthotonus, spasticity or flaccidity and seizures. Retinal haemorrhages and the classic cherry red skin colour are seldom seen. Different people and populations may have different carbon monoxide tolerance levels. On average, exposures at 100 ppm or greater is dangerous to human health.

Treatment and prevention : The mainstay of treatment is 100% oxygen administration until the COHb level is normal. When the patient is stable enough to be transported, hyperbaric oxygen (HBOT) should be considered. This treatment is safe and well tolerated.

Public education about the danger of carbon monoxide, with emphasis on safety in the home and workplace, is the key to effective prevention. This could be achieved through a media campaign when risk is greatest, i.e. during the winter. Close liaison between public health physicians and leaders of building, gas and home heating industries is a prerequisite for an effective prevention strategy.

Key Words : Carbon Monoxide, Hyperbaric Oxygen Therapy, Carboxyhaemoglobin (COHb)

Introduction

Carbon monoxide is known as the silent killer, being colorless, odourless, and tasteless. Initially non-irritating, it is very difficult for people to detect. Carbon monoxide is a product of incomplete combustion of organic matter due to insufficient oxygen supply that prevents complete oxidation of carbon to CO2. Its density is 0.97 of that of air.

The deadly effect of carbon monoxide was known as long ago as Greek and Roman times,[1] when the gas was used for executions. In 1857 Claude Bernard postulated that its noxious effect

[a]Classified Specialist (Marine Medicine) INHS Dhanwantari, Port Blair. [b]Senior Advisor (Marine Medicine) IHQ MOD, New Delhi. [a]Corresponding author : kamalmishra@rediffmail.com; Mob. : +91-08800783322.

was caused by reversible displacement of oxygen from haemoglobin forming Carboxyhaemoglobin (COHb).[2] In 1926 it became apparent that hypoxia was caused not only by deficient oxygen transport but also by poor tissue uptake. Warberg used yeast cultures to show that cellular uptake of oxygen was inhibited by exposure to a large amount of carbon monoxide.[3]

History And Epidemiology

During World War II, Nazis used gas vans to kill an estimated over 700,000 prisoners by carbon monoxide poisoning. This method was also used in the gas chambers of several death camps such as Treblinka, Sobibor and Belzec. Gassing with carbon monoxide started in the euthanasia programme developed by the Nazis to murder the mentally ill and disabled people before the war started in earnest. Exhaust fumes from tank engines were used to supply the gas to the chambers.

The true number of incidents of carbon monoxide poisoning is unknown, since many non-lethal exposures go undetected. From the available data, carbon monoxide poisoning is the most common cause of injury and death due to poisoning worldwide.

Each year in Britain about 50 people die and 200 are severely injured by carbon monoxide poisoning.[4] Some poisonings are caused by self-harm but most are accidental.[5] It is the commonest cause of accidental poisoning in the world. In the 1960s and 1970s the conversion from coal gas to carbon-monoxide-free natural gas caused a dramatic reduction in poisoning incidents.[6] In UK most accidents arise through central heating faults. By contrast, in the USA most deaths are caused by inhalation of exhaust fumes.

It has been estimated that more than 40,000 people per year seek medical attention for carbon monoxide poisoning in the United States. The CDC reports, "Each year, more than 500 Americans die from unintentional carbon monoxide poisoning, and more than 2,000 commit suicide by intentionally poisoning themselves.

Sources

Carbon monoxide is produced endogenously in small amounts as a byproduct of haem catabolism. Together with nitric oxide it affects cellular function and acts as a neurotransmitter.

Environmental carbon monoxide is produced by incomplete combustion of any organic fuel. It is often produced in domestic or industrial settings in motor vehicles, gas heaters, and cooking equipment that are powered by carbon based organic fuels.

Carbon monoxide poisoning is often associated with malfunctioning or obstructed exhaust systems and with suicide attempts. When cars, trucks, or other engines are left running in enclosed spaces, such as garages, CO levels can build up and leak back into the house. Even sitting in an idling car in an open garage or swimming behind an idling boat could be dangerous. Poisoning may also occur following the use of a self-contained underwater breathing apparatus (SCUBA) due to faulty diving air compressors. Another source of poisoning is exposure to the organic solvent dichloromethane (methylene chloride), found in some paint removers. Dichloromethane produces carbon monoxide on being metabolized.

Clinical Signs And Diagnosis

The signs of carbon monoxide poisoning vary with concentration and length of exposure. Subtle cardiovascular or neurobehavioural effects occur at low concentration. The onset of chronic poisoning is usually insidious and easily mistaken for viral prodrome, depression, or gastroenteritis in children. Other family members may also demonstrate similar symptoms.

The initial symptoms of acute carbon monoxide poisoning include headache, nausea, malaise, and fatigue as in viral infection. Headache is the most common symptom of acute carbon monoxide poisoning; it is often described as dull, frontal, and continuous. Increasing exposure produces cardiac abnormalities including tachycardia, hypotension and arrhythmias. The major manifestations of carbon monoxide poisoning develop in the organ systems most dependent on oxygen use, the central nervous

system and the heart.

Neurological signs include disorientation, visual disturbances, syncope, delirium, hallucinations, dizziness, unsteady gait, seizures, stroke, loss of conciousness, respiratory arrest, and death. Infants may be irritable and feed poorly.

Cardiac manifestation of acute carbon monoxide poisoning include angina, palpitations, arrhythmias, atrial fibrillation, pulmonary edema, mottled skin lesions due to decreased circulation, poor capillary refill, hypotension and visual and auditory problems.

One of the major concerns following acute carbon monoxide poisoning is the severe[14] delayed neurological syndrome (DNS). Problems include difficulty with higher intellectual functions, short-term memory loss, dementia, amnesia, psychosis, irritability, gait and speech disturbances, Parkinson's like syndromes, cortical blindness, and a depressed mood. These delayed neurological sequelae may occur in up to 50% of patients after 3 to 40 days of apparent recovery. It is difficult to predict who will develop delayed sequelae; however, advanced age, loss of consciousness during initial presentation, and initial neurological abnormalities may increase the chance of developing DNS. Some of the neurological signs such as parkinsonism are easily detected. Personality, cognitive and memory changes are not readily apparent and can be missed unless specifically targeted. Headaches, weakness, apraxia, aphasia, rigidity, and fecal and urinary incontinence can be part of DNS. Children may present with behavioral or education problems. Most neuropsychiatric signs resolve within a year.

The classic sign of carbon monoxide poisoning is actually more often seen in the dead than the living is appearing red-cheeked and healthy. Cherry pink colour develops in nails, skin and mucosa.

In **acute poisoning**, common abnormalities of posture and tone are cogwheel rigidity, opisthotonus, spasticity or flaccidity and seizures. Retinal haemorrhages and the classic cherry red skin colour are seldom seen. A rise in creatine phosphokinase follows muscle necrosis.

Chronic Poisoning

Breathing low levels of carbon monoxide over a long period can cause severe persistent headaches, lightheadedness, depression, confusion, memory loss, and brain damage. Clues to diagnosis are dyspnoea, nausea and headaches when person is indoors and symptoms usually resolving when person is removed from exposure, i.e. when he leaves the building, and becoming worse on return. Other people and pets in the building also demonstrate the same symptoms. Long-term exposures to carbon monoxide present the greatest risk to persons with coronary heart disease and in females who are pregnant.

Carbon monoxide poisoning is diagnosed by measuring COHb in a heparinized blood sample (arterial or venous). The bed side test for COHb is done by taking 01 ml of patient's blood and adding 10 ml of distilled water and 01 ml of 5% sodium peroxide. If the solution turns straw yellow (COHb <20%) or turns pink (COHb>20%), It indicates present of COHb.

Symptoms usually begin when the concentration rises above 10%. There is a poor correlation between the blood level and the clinical condition. In normal non-smokers, the average is about 1%, rising to 15% in heavy smokers. Levels of 5% are found in patients of haemolytic anaemias and pregnancy. Pulse oximeters are not suitable for the diagnosis of carbon monoxide poisoning. The wavelength of most cannot distinguish between oxyhaemoglobin and COHb. A carbon monoxide breath-analyser is a simple bedside screening test but its practical value is limited by numerous confounders such as smoking and alcohol consumption.

The fetus is particularly vulnerable to carbon monoxide poisoning. Fetal haemoglobin shifts the oxygen-haemoglobin dissociation curve to the left. Chronic exposure to carbon monoxide in pregnancy causes growth retardation, fetal distress and fetal death. Surviving neonates may have developmental disorders and brain damage. The risk is compounded by smoking in pregnancy. In the first months of infancy, while fetal haemoglobin is raised, the risk is greater. People with sickle cell anaemia and thalassaemia who have a raised fetal haemoglobin are at excess risk.

Carbon monoxide is not toxic to all forms of life. Its harmful effects are due to binding with hemoglobin. It thus has no effect on photosynthesizing plants. Different people and populations may have different carbon monoxide tolerance levels. On average, exposures at 100 ppm or greater is dangerous to human health. In the USA, the OSHA (Occupational safety and health administration) limits long-term workplace exposure levels to less than 50 ppm averaged over an 8-hour period; in addition, employees are to be evacuated from confined spaces if an upper limit ("ceiling") of 100 ppm is reached. The carbon monoxide tolerance level for any person is altered by several factors, including activity levels, rate of ventilation, a pre-existing cerebral or cardiovascular disease, cardiac output, anemia, sickle cell disease , barometric pressure, and metabolic rate. [7,8,9]

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

Table 1: Symptoms of Acute CO Poisoning based on blood COHb Levels

Carboxyhaemoglobin level	Clinical features
<10%	Very few, mainly headache
10-20%	Dyspnoea on exertion, lethargy, nausea, chest pain, tightness around forehead
20-30%	Headache, irritability, fatigue, nausea, vomiting, disturbed judgement, vision and vertigo
40-50%	Severe headache, confusion and collapse
50-60%	Same as above plus syncope, Cheyne-Stroke breathing, fits
60-70%	Coma, seizures, respiratory failures and death, weak thready pulse and slow breathing
70%	Rapidly fatal

The acute effects produced by carbon monoxide in relation to ambient concentration in parts per million are listed below :

Lab investigations

Carbon monoxide may be quantified in blood using spectrophotometric methods or chromatographic techniques in order to confirm a diagnosis of poisoning in a person. This method also assists in the forensic investigation of a case of fatal exposure. COHb blood saturations may range up to 10% in heavy smokers or persons extensively exposed to automotive exhaust gases. In symptomatic poisoned people they are often in the 10–30% range, while persons who succumb may have postmortem blood levels of 30–90%.

The ratio of COHb to hemoglobin molecules in an average person may be up to 5%, although cigarette smokers who smoke two packs/day may have levels up to 9%.

Finger tip COHb saturation monitor (SpCO%). Note: This is not the same as a pulse oximeter (SpO2%), although some models (such as this one) do measure both the oxygen and carbon monoxide saturation.[10]

Breath CO monitor displaying carbon monoxide concentration of an exhaled breath sample (in ppm) with its corresponding percent concentration of COHb.

A CO-oximeter is used to determine COHb levels. Pulse CO-oximeters estimate COHb with a non-invasive finger clip similar to a pulse oximeter. These devices function by passing various wavelengths of light through the fingertip and measuring the light absorption of the different types of hemoglobin in the capillaries.

The use of a regular pulse oximeter is not effective in the diagnosis of carbon monoxide poisoning as people suffering from carbon monoxide poisoning may have a normal oxygen saturation level on a pulse oximeter due to the fact that COHb is misrepresented as oxyhemoglobin.

Breath CO monitoring offers a viable alternative to pulse CO-oximetry. COHb levels have been shown to have a strong correlation with breath CO concentration. However, many of these devices require the user to inhale deeply and hold their breath to allow the CO in the blood to diffuse into the lungs before the measurement can be made. As this is not possible in a nonresponsive patient, these devices are not appropriate for use in on-scene emergency care detection of CO poisoning.

Differential Diagnosis

There are many conditions to be considered in the differential diagnosis of carbon monoxide poisoning. The earliest symptoms, especially from low level exposures, are often non-specific and readily confused with other illnesses, typically flu-like viral syndromes, depression, chronic fatigue syndrome, and migraine. Carbon monoxide has been called a **"great mimicker"** due to the fact that presentation of CO poisoning is diverse and nonspecific. Other conditions included in the differential diagnosis include acute respiratory distress syndrome, altitude sickness, lactic acidosis, diabetic ketoacidosis, meningitis, methemoglobinemia, alcohol intoxication.

WHO Recommendations

The following guideline values (ppm values rounded) and periods of time-weighted average exposures have been determined in such a way that the COHb level of 2.5% is not exceeded, even when a normal subject engages in light or moderate exercise:

- 100 mg/m3 (87 ppm) for 15 min
- 60 mg/m3 (52 ppm) for 30 min
- 30 mg/m3 (26 ppm) for 1 h
- 10 mg/m3 (9 ppm) for 8 h

For indoor air quality 7 mg/m3 (6 ppm) for 24 h so as not to exceed 2% COHb for chronic exposure)

Pathophysiology

The precise mechanisms, by which the effects of carbon monoxide are induced upon bodily systems, are complex and not yet fully understood. Known mechanisms include carbon monoxide binding to hemoglobin, myoglobin, mitochondrial cytochrome oxidase, restricting oxygen supply, and carbon monoxide causing brain lipid peroxidation. Activation of inflammatory process lead to neurological damage.

Carbon monoxide has a higher diffusion coefficient compared to oxygen. When CO is not ventilated it binds to hemoglobin, which

is the principal oxygen-carrying compound in blood; this produces a compound known as carboxyhemoglobin (COHb). The traditional belief is that carbon monoxide toxicity arises from the formation of COHb, which decreases the oxygen-carrying capacity of the blood and inhibits the transport, delivery, and utilization of oxygen by the body. The affinity between hemoglobin and carbon monoxide is approximately 250 times stronger than the affinity between hemoglobin and oxygen (HbO2) hence hemoglobin binds to carbon monoxide in preference to oxygen.

Hemoglobin

Hemoglobin is a tetramer with four oxygen binding sites. The binding of carbon monoxide at one of these sites increases the oxygen affinity of the remaining three sites, which causes the hemoglobin molecule to retain oxygen that would otherwise be delivered to the tissue. This situation is described as carbon monoxide shifting the oxygen dissociation curve to the left. Because of the increased affinity between hemoglobin and oxygen during carbon monoxide poisoning, little oxygen will actually be released in the tissues. This causes hypoxic tissue injury. Hemoglobin acquires a bright red color when converted into COHb, so poisoned cadavers acquire an unnatural reddish hue.

Pregnancy

Carbon monoxide poisoning in pregnant women may cause severe adverse fetal effects. Poisoning causes fetal tissue hypoxia by decreasing the release of maternal oxygen to the fetus. Carbon monoxide also crosses the placenta and combines with fetal hemoglobin, causing more direct fetal tissue hypoxia. In addition, fetal hemoglobin has a 10 to 15% higher affinity for carbon monoxide than adult hemoglobin, causing more severe poisoning in the fetus than in the adult. Elimination of carbon monoxide is slower in the fetus, leading to an accumulation of the toxic chemical. The level of fetal morbidity and mortality in acute carbon monoxide poisoning is significant, so despite mild maternal poisoning or following maternal recovery, severe fetal poisoning or death may still occur. [11]

Treatment and Prognosis

The mainstay of treatment is 100% oxygen administration until the COHb level is normal. When the patient is stable enough to be transported, hyperbaric oxygen (HBOT) should be considered. This treatment is safe and well tolerated, the main complication being ear barotrauma. The time-frame within which hyperbaric oxygen is most effective is not known. In one large retrospective study it was not effective if started after 6 hours. [12]

In 1895, Haldane demonstrated that a mouse could be kept alive by exposure to hyperbaric oxygen at the same time as carbon monoxide. This seminal experiment proved that enough oxygen for survival could be transported in solution when transport by haemoglobin was severely impaired.

Hyperbaric Oxygen Therapy

HBOT has many benefits. The half-life of Carboxyhaemoglobin (COHb) at 3 ATA (absolute atmospheres) of oxygen is only 23 minutes. With 100% O2 therapy, the half-life of COHb is 74 minutes, compared to 320 minutes while breathing room air. Other benefits of HBOT are improved mitochondrial function, impairment of platelet adhesion in the capillaries and inhibition of lipid peroxidation. A patient with mild symptoms will require NBO (normobaric oxygen therapy) for 4-6 hour for COHb level to come down to 5%. [15]

There have been six randomized controlled trials in which the two treatment options have been compared; Four RCTs found hyperbaric oxygen improved outcome and two found no benefit for hyperbaric oxygen.

In the absence of firm evidence most centres continue using hyperbaric oxygen if the COHb is above 25-30%. Myocardial ischaemia and neurological signs, especially coma, are treated with HBOT, irrespective of the concentration. There is general agreement that prolonged hyperbaric oxygen is the treatment of choice in pregnancy. This is because in fetus COHb levels are higher and clearance slower than in the mother.

Standard Operating Procedures

Initial treatment for carbon monoxide poisoning is to immediately remove the person

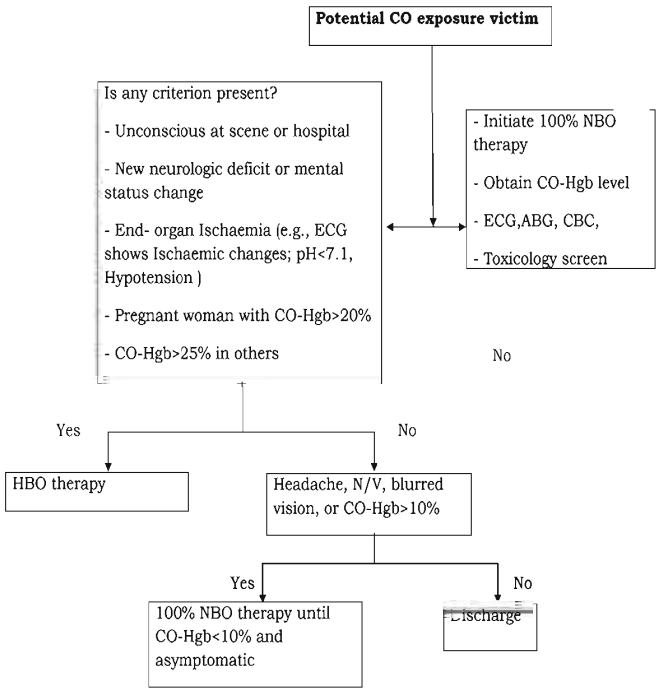
from the exposure. Those who are unconscious may require CPR on site.

Consider immediate transfer of patients with COHb levels above 25-40% or cardiovascular or neurologic impairment to a hyperbaric facility, if feasible. Persistent impairment after 4 hours of normobaric oxygen therapy (NBO) necessitates transfer to a hyperbaric center. Pregnant patients should be considered for hyperbaric treatment at lower COHb levels.

Continue therapy until the patient is asymptomatic and HbCO levels are below 10%. In patients with cardiovascular or pulmonary compromise, lower thresholds of 2% have been suggested.

RECOMPRESSION AS PER TABLE 60 OF INBR 2806				
	RATE	DEPTH MSW	BREATHING MIXTURE	DURATION
DESCENT	FAST	18 MTRS	O_2	25 MIN
STOP		18 MTRS	AIR	05 MIN
		18 MTRS	O_2	25 MIN
ASCENT		18 MTRS	AIR	05 MIN
		18-0 MTRS	O_2	30 MIN
			TOTAL	**01 HR 30 MINS**

MANAGEMENT ALGORITHM OF ATIENTS WITH CO POISONING



Serial neurologic examinations, including fundoscopy, CT scans, and, possibly, MRI, are important in detecting the development of cerebral edema. Cerebral edema requires intracranial pressure (ICP) and invasive blood pressure monitoring to further guide therapy. Head elevation, mannitol, and moderate hyperventilation to 28-30 mm Hg PCO2 are indicated in the initial absence of ICP monitoring. Acidosis with pH above 7.[15] is helpful because it results in a rightward shift in the oxyhemoglobin dissociation curve, increasing tissue oxygen availability. Acidosis generally improves with oxygen therapy.

Prevention

Public education about the danger of carbon monoxide, with emphasis on safety in the home and workplace, is the key to effective prevention. This could be achieved through a media campaign when risk is greatest, i.e. during the winter. Close liaison between public health physicians and leaders of building, gas and home heating industries is a prerequisite for an effective prevention strategy. Such collaboration ensures safety through proper standards for home ventilation, central heating installation and maintenance. Cheap battery operated carbon monoxide detectors are now widely available. They should be installed in homes and in places such as garages where people are at risk from exhaust fumes. In old properties, particularly where there is solid fuel heating, carbon monoxide detectors should be located in sleeping areas.

Conclusion

Overall, Carbon monoxide is the most common dangerous contaminant. This is most perilous when the air is otherwise clean because carbon monoxide is odourless and tasteless. Contaminants in compressed gas may have been present in the gas before compression, added during compression or are resident in the storage system. There is a possibility of increasing the concentration of trace contaminants when using recycled gases for deep diving operations. The compounds that are not removed in any purification process can accumulate with recycling. For this reason, a thorough risk analysis should be done to determine all likely contaminants. With an increase in depth, and hence partial pressure of contaminants, the toxicity increases. Hence a suitable screening gas analysis program for the

identified contaminants is highly desirable and recommended.

How to cite the article

Mishra K, Krishnan G. Carbon Monoxide Poisoning. *J. Marine Medical Society,* 2016, 18 (2) : 179-186.

Source of support

Nil

Conflicts of interest

All authors have none to Declare.

References

1. Ganong WF. Review of Medical Physiology. Norwalk Ct: Appleton & Lange, 1995
2. Bernard C. Le Cons Sur les Effets des Substances Toxiques et Médicamenteuses. Paris : Bailliere, 1857
3. Warburg O. Über die Wirkung des Kohlenoxyds auf den Stoffwechsel der Hefe. Biochem Z 1926;177: 471
4. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning — a public health perspective. Toxicology 2000; 145 : 1-14
5. Guy KM, Pimlott JK, Rogers M, Cross M. The new CO and smoke inhalation advisory service in the UK. Treatment of poisoning. Indoor Built Environment 1999;8: 199-202
6. Anonymous. Carbon monoxide, an old enemy forgot. Lancet 1981; ii : 75-6
7. Raub JA, Mathieu-Nolf M, Hampson NB, Thom SR. Carbon monoxide poisoning — a public health perspective. Toxicology 2000; 145 : 1-14
8. Thom S R, Fisher D, Xu YA, Notarfrancesco K, Ischiropoulos H. Adaptive responses and apoptosis in endothelial cells exposed to carbon monoxide. Proc Natl Acad Sci USA 2000; 97: 1305-10
9. Ernst A, Zibrak J D. Carbon monoxide poisoning. N Engl J Med 1998; 339 : 1603-8
10. Hampson NB. Pulse oximetry in severe carbon monoxide poisoning. Chest 1998;114: 1036-41
11. Aubard Y, Magne I. Carbon monoxide poisoning in pregnancy. Br J Obstet Gynaecol 2000;107: 833-8
12. Weaver LK, Howe S, Hopkins R, Chan KJ. Carboxy hemoglobin half-life in carbon monoxide-poisoned patients treated with 100% oxygen at atmospheric pressure. Chest 2000;117: 801-8
13. Juurlink DN, Stanbrook MB, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. Cochrane Database Syst Rev 2000;2: CD00204
14. Choi IS. Delayed neurologic sequelae in carbon monoxide intoxication. Arch Neurol 1983;40: 433-5
15. Raphael JC, Elkharrat D, Jars-Guincestre MC et al. Trial of normobaric and hyperbaric oxygen for acute carbon-monoxide intoxication. Lancet 1989; ii : 414-19