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Carbon monoxide poisoning in pregnancy and paediatric patients: proposal of a clinical management algorithm.

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Keypoints

The authors propose an algorithm about the clinical management of carbon monoxide poisoning in pregnancy and paediatric patients.

Abstract

Carbon monoxide poisoning remains one of the most frequently underdiagnosed conditions. Due to the absence of pathognomonic signs and symptoms, accurate diagnosis relies on comprehensive history-taking and contextual assessment, including environmental exposure and clinical presentation.

The extent of foetal damage caused by CO exposure is closely associated with gestational age. At present, no dedicated clinical guidelines specifically address the management of CO poisoning during pregnancy or in paediatric patients.

In this context, the delivery of effective treatment is frequently impeded by systemic factors, including organisational constraints, infrastructure limitations, and logistical challenges.

Keywords

Carbon monoxide poisoning, CO intoxication, hyperbaric oxygen therapy, CO management, hyperbaric chamber, pregnancy-related CO poisoning, maternal CO exposure, fetal hypoxia due to CO, paediatric CO intoxication, child, infant.

Introduction

Carbon monoxide (CO) is a colourless, odourless, tasteless, and non-irritating gas, typically present in the atmosphere at concentrations below 0.001%. It may be produced endogenously through haemoglobin catabolism or exogenously via incomplete combustion of carbon-based compounds.

Although relatively uncommon, CO poisoning remains the leading cause of toxic exposure in developed countries and can result in significant morbidity and mortality.

Diagnosis is frequently missed due to non-specific symptoms, as a result, the true incidence of carbon monoxide poisoning is likely underestimated—particularly in pregnancy.

In the Italian context, carbon monoxide poisoning represents a significant cause of toxic exposure, with approximately 93% of cases attributed to accidents. National estimates indicate around 600 fatalities annually, with two-thirds linked to intentional exposure.

The estimated incidence of CO poisoning is approximately 20 cases per 100,000 population, with a reported case fatality rate of 5.8%. The majority of exposures (approximately 80%) occur in domestic environments, typically associated with malfunctioning heating appliances such as stoves and boilers. The gender distribution is nearly equal, with males accounting for 51% of cases and females 49%. Pregnant women represent approximately 2.3% of the total population affected by CO poisoning, while individuals under the age of 12 constitute around 18%. Seasonal variation is evident, with the highest incidence observed during the winter months—specifically November through February—corresponding to increased use of indoor heating systems.

It is important to note that many cases, particularly those that are asymptomatic or present with mild symptoms, are likely underreported. Consequently, the true burden of CO poisoning may be significantly underestimated. Data on CO exposure during pregnancy remain limited, and most paediatric cases are attributed to accidental causes.

Another factor contributing to the underestimation of carbon monoxide poisoning in Italy is the lack of a centralised national registry, which leads to fragmented and inconsistent epidemiological data. Available figures are often based on sporadic reporting from a limited number of clinical centres, without systematic surveillance. In particular, data on exposure during pregnancy—whether accidental or intentional—remain extremely scarce.

Pathophysiological basis

Carbon monoxide (CO) poisoning typically occurs through inhalation. Once inhaled CO binds with haemoglobin, forming carboxyhaemoglobin (COHb), a compound with an affinity for haemoglobin approximately 200–300 times greater than that of oxygen.

This binding significantly impairs the haemoglobin's ability to transport oxygen to peripheral tissues, resulting in a leftward shift of the oxygen-haemoglobin dissociation curve and subsequent tissue hypoxia.

Carbon monoxide toxicity is mediated through two primary mechanisms:

- Tissue hypoxia (Representing the indirect form of injury)
- Inflammation and cellular disruption (Representing the direct form of injury)

Initial injury in carbon monoxide poisoning is primarily driven by tissue hypoxia, resulting from reduced arterial oxygen content and impaired oxygen delivery. This hypoxic state triggers oxidative stress and the production of reactive oxygen species (ROS), initiating a biochemical cascade that leads to widespread inflammation and cellular damage.

The second mechanism of injury in carbon monoxide poisoning involves direct cellular toxicity, primarily driven by inflammatory responses induced by CO itself. This is mediated through several biochemical interactions, including:

- **Binding to cytochrome enzymes** (e.g., cytochrome A3, cytochrome P450) which reduces ATP synthesis (histotoxic hypoxia).
- **Binding to myoglobin**, impairing cardiac contractility, causing hypotension, arrhythmias, and worsening systemic hypoxia.
- **Nitrite production**, leading to vasodilation, reduced venous return, and compromised myocardial perfusion.

- **Activation of guanylate cyclase**, causing hypotension, hypoperfusion and cerebral oedema.
- **Leukocyte adhesion to cerebral microvascular endothelium**, triggering immune-mediated CNS damage.
- **Lipid peroxidation and myelin basic protein (MBP) alteration**, contributing to cerebral autoimmunity.
- **Inhibition of endogenous antioxidant defence mechanisms.**

Carbon monoxide readily crosses the placental barrier, resulting in a leftward shift of the foetal oxygen-haemoglobin dissociation curve and subsequent tissue hypoxia. The extent of CO diffusion increases with gestational age and foetal weight, and is influenced by factors such as placental blood flow and maternal haemoglobin concentration.
Foetal hypoxia arises through two primary mechanisms:

- Maternal hypoxaemia: where reduced arterial oxygen levels lead to diminished placental oxygen delivery
- Trans-placental transfer of CO

Hyperbaric oxygen therapy (HBOT) offers significant therapeutic benefits in this context, including:

- Accelerated dissociation of CO from haemoglobin
- Accelerated dissociation from mitochondrial respiratory chains
- Increased levels of dissolved oxygen in the bloodstream
- Reduction of hypoxic tissue injury

HBOT reduces the half-life of CO from approximately 60 minutes to 23 minutes, facilitates more rapid symptom resolution, and lowers the risk of delayed neurological sequelae.

According to the 2015 SIMSI guidelines, the following criteria are recommended for access to hyperbaric oxygen therapy:

- Coma
- Altered level of consciousness
- Neuropsychiatric symptoms attributable to carbon monoxide poisoning
- Decompensated metabolic acidosis
- Chest pain and/or signs of myocardial ischaemia
- Arrhythmias
- Pregnancy
- Age under six months due to the presence of foetal haemoglobin (HbF)

Although the carboxyhaemoglobin (COHb) level is useful for confirming exposure, it is not a reliable indicator of clinical severity. Nonetheless, treatment is recommended in the following cases:

- Asymptomatic patients with COHb >25%
- Asymptomatic children under 12 years of age with COHb >10%
- Asymptomatic patients with a history of myocardial ischaemia and COHb >15%
- All pregnant women, regardless of symptom severity or COHb level

Absolute contraindications to hyperbaric therapy include untreated pneumothorax, PaO_2/FiO_2 ratio <200, claustrophobia (particularly in unsedated or conscious patients), acute psychiatric decompensation, and status epilepticus. Relative contraindications should be assessed on a case-by-case basis. A thorough evaluation of the risk–benefit ratio is essential prior to initiating treatment.

Clinical presentation and diagnosis

Carbon monoxide poisoning does not present with pathognomonic signs or symptoms. Consequently, diagnosis relies heavily on a thorough clinical history and careful

evaluation of circumstantial factors. The clinical presentation is often heterogeneous and characterised by highly non-specific symptoms, which may lead to misdiagnosis or delays in treatment (see Table 1).

In more severe cases, symptoms may involve multiple organ systems:

Cardiovascular: retrosternal chest pain, arrhythmias, signs of myocardial ischaemia, myocardial infarction, cardiac arrest

Neurological: dizziness, visual disturbances, ataxia, confusion, loss of consciousness, seizures, cerebral ischaemia, coma

Metabolic: severe acidosis with increased anion gap

Musculoskeletal: rhabdomyolysis

Respiratory: dyspnoea and/or tachypnoea; in severe cases, pulmonary oedema and respiratory depression

Renal: acute kidney injury secondary to rhabdomyolysis

Gastrointestinal: intestinal ischaemia

Gynaecological: miscarriage

The severity of clinical manifestations is generally related to the concentration of carbon monoxide in the environment and the duration of exposure. However, symptom intensity does not correlate directly with poisoning severity.

Clinical presentation is influenced by blood levels of carbon monoxide and carboxyhaemoglobin (COHb), as well as the vulnerability of target organs.

Diagnostic thresholds for COHb are >5% in non-smoking adults and children, and >10% in smokers. Based on COHb levels, poisoning may be classified as:

- Mild: <10%
- Moderate: 10–25%
- Severe: >25%

Historically, this classification was used to guide treatment decisions. However, it does not reliably predict prognosis, nor does it correlate with the extent of neurological damage.

SEVERITY CLASS	SIGNS AND SYMPTOMS	
Grade 1: Asymptomatic (*)	None	
Grade 2: Mild	Headache Dizziness	Nausea Vomiting
Grade 3: Moderate	Confusion Cognitive slowling Weakness Ataxia Behavioral changes Alterations in psychometric test performance	Dyspnea on exertion Tachypnea Tachycardia Palpitations Hypoacusis Blurred vision
Grade 4: Severe	Stupor Coma Seizures Syncope Disorientation Abnormal findings on brain CT scan Hypotension/shock Rhabdomyolysis	Chest pain Palpitations Arrhythmias ECG signs of myocardial ischaemia Pulmonary oedema Lactic acidosis Skin blisters Cardiac arrest

Table 1. Clinical Signs and Symptoms by Severity. * Patients with positive COHb levels.

In pediatric patients, the symptoms observed following exposure to CO are also related to the patient's age group (see Table 2).

<table>
<tr><th>Grading</th><th colspan="3">Signs and symptoms categorised by age</th></tr>
<tr><td></td><td>0 - 2 years</td><td>3 -7 years</td><td>8 - 14 years</td></tr>
<tr><td>Grade 1</td><td colspan="3">Asymptomatic</td></tr>
<tr><td rowspan="3">Grade 2</td><td colspan="3">Nausea (accompanied by retching)
Vomiting
Diarrhoea</td></tr>
<tr><td>Irritability
Inconsolable crying
Feeding refusal</td><td colspan="2">Abdominal pain, with or without diarrhoea</td></tr>
<tr><td colspan="2"></td><td>Vertigo</td></tr>
<tr><td rowspan="2">Grade 3</td><td colspan="3">In addition to the previous symptoms:
Tachypnoea (without distress, nasal flaring, or sternal retraction)
Behavioural abnormalities
Reported alterations in consciousness (transient loss of consciousness, somnolence, stupor, coma)
Reported seizures
Ataxia</td></tr>
<tr><td>Prolonged capillary refill
Hyporeactivity
Whimpering cry</td><td colspan="2">Disorientation
Tachycardia
Visual disturbances
Chest pain</td></tr>
<tr><td>Grade 4</td><td colspan="3">Tachypnoea with signs of respiratory fatigue
Syncope
Seizures
Altered state of consciousness (somnolence, lethargy, coma)
Cardiac Arrest</td></tr>
<tr><td></td><td colspan="3">In Case of Exposure to Fire Smoke, in Addition to the Symptoms Previously Described, Also Consider:
• Presence of soot deposits on the skin and at the airway entry points (oral cavity and nostrils)
• Severe haemodynamic instability
• Resumption of cardio-respiratory activity following cardiac arrest (PALS protocol) Priority should be given to antidotal treatment</td></tr>
</table>

Table 2. Classification by Grade Based on Symptomatology (Modified from: Locatelli, 2000; Macnow, 2016)

Foetal injury does not correlate directly with the severity of maternal signs and symptoms; rather, foetal physiology plays a crucial and determining role.

The effects that CO poisoning may have on the fetus depend on the gestional age (Table 3). Fetal damage does not directly correlate with the severity of maternal signs and symptoms of intoxication an important and essential role is played by phetal physiology.

PREGNANCY PERIOD	EFFECTS OF CO
First Trimester	Telencephalic dysgenesis, Anoxic encephalopathy, Childhood behavioural issues, Cerebellar volume reduction (in animal studies), Limb malformations, Limb agenesis, Hip dysplasia/subluxation, Maxillary atresia
Second–Third Trimester	Low birth weight, Psychomotor delay, Cerebral atrophy, Seizures, Spasticity, Intrauterine death
Birth	Increased risk of sudden neonatal death

Table 3. Effects of carbon monoxide listed for gestational age

Discussion

Diagnostic and Therapeutic Pathway

At present, there are no clinical guidelines specifically addressing the management of carbon monoxide poisoning in pregnant women or paediatric patients. This absence of recommendations presents a significant challenge for healthcare professionals, who must often face organisational, logistical, and infrastructural limitations—particularly due to the uneven distribution and limited accessibility of hyperbaric facilities across the country.

Hyperbaric oxygen therapy in pregnant women constitutes a time-critical intervention and should be initiated within six hours of exposure, or as early as clinically feasible.

Pre-Hospital Management

The safety of healthcare personnel must be prioritised at all stages of intervention. The patient should be promptly removed from the site of exposure and placed in a safe environment. Immediate clinical assessment following the ABCDE approach is required, alongside vascular access placement and vital sign monitoring and support.

A comprehensive clinical history should be obtained, with attention to environmental and circumstantial factors. In cases involving unconscious patients, those with neurological symptoms, or paediatric patients, input from family members or witnesses is essential.

High-flow normobaric oxygen therapy with FiO_2 100% should be initiated as early as possible Administration should be via a non-rebreather mask or, where indicated, through an endotracheal tube in intubated patients.

Transport

Hospital transfer should be carried out safely and without delay. Ideally, the patient should be taken to a facility equipped with obstetric/gynaecological, paediatric, and intensive care services, provided this does not significantly prolong transfer time or delay treatment.

Oxygen therapy should be continued throughout transport.

In-Hospital Management

- Repeat clinical reassessment using the ABCDE approach, implement appropriate interventions were indicated (e.g., intubation, life support)
- High-flow normobaric oxygen therapy (FiO_2 100%) must be continued without interruption.
- Perform a detailed history-taking and symptom staging (Grades 1–4; see Tables 1–2)
- Initiate diagnostic investigations including Arterial blood gas analysis and laboratory tests (full blood count, liver and renal function, LDH, myoglobin)
- Measure of COHb levels: diagnostic thresholds are >5% in non-smoking pregnant women and paediatric patients, and >10% in smokers
- Classify poisoning severity based on COHb levels: mild <10%, moderate 10–25%, severe >25%
- Evaluate for respiratory acidosis and lactate levels, which may reflect tissue hypoxia
- Request ECG and cardiology consultation; if ECG is abnormal, assess troponin I, CPK-MB, and perform echocardiography
- Request for Obstetric/gynaecological evaluation for emergencies and treatment planning; paediatric/neonatal assessment as appropriate
- Initiate multidisciplinary consultation, including hyperbaric specialists

Engagement with the hyperbaric centre is essential to evaluate indications, contraindications, and the risk–benefit profile of treatment. Absolute contraindications include untreated pneumothorax, PaO_2/FiO_2 ratio <200, status epilepticus, claustrophobia, and acute psychiatric decompensation. Relative contraindications should be evaluated on a case-by-case basis, particularly in relation to maternal and foetal safety.

All pregnant women, in the absence of contraindications, should undergo hyperbaric therapy regardless of poisoning severity. Children under 12 years of age should be treated if COHb >10%, even if asymptomatic. Patients with PaO_2/FiO_2 <200 are excluded from hyperbaric oxygen therapy.

Hyperbaric Centre Management

Transfer to the hyperbaric facility must be organized under protected conditions, with continued administration of high-flow normobaric oxygen. Treating conscious paediatric patients may be challenging due to the chamber environment hence, parental presence is recommended to improve compliance, where feasible.

Hospitals should be encouraged to develop internal protocols to support this approach.

Particular attention must be paid to critically ill patients, including the management of airway devices, drainage systems, infusion pumps, mechanical ventilation, monitoring equipment, and fluid therapy.

Current hyperbaric treatment protocols vary in duration and pressure, typically ranging from 1.9 ATA (193 kPa) to 2.8 ATA (284 kPa).

Post-Treatment Follow-Up

Post-treatment follow-up, (with particular emphasis on obstetric and gynaecological monitoring), is essential.

Recommended evaluations include serial assessment of: Cardiac biomarkers, EEG, and ECG at 12, 24, and 48 hours after treatment. Echocardiography should be performed at 24 hours, and neuropsychological testing is advised.Patients should be monitored over the following months for potential neuropsychiatric sequelae. Comprehensive follow-up involving obstetric, gynaecological, paediatric and neonatal specialists is critical to ensure optimal outcomes.

At the end of these considerations, the authors propose the algorithm shown in Figure 1.

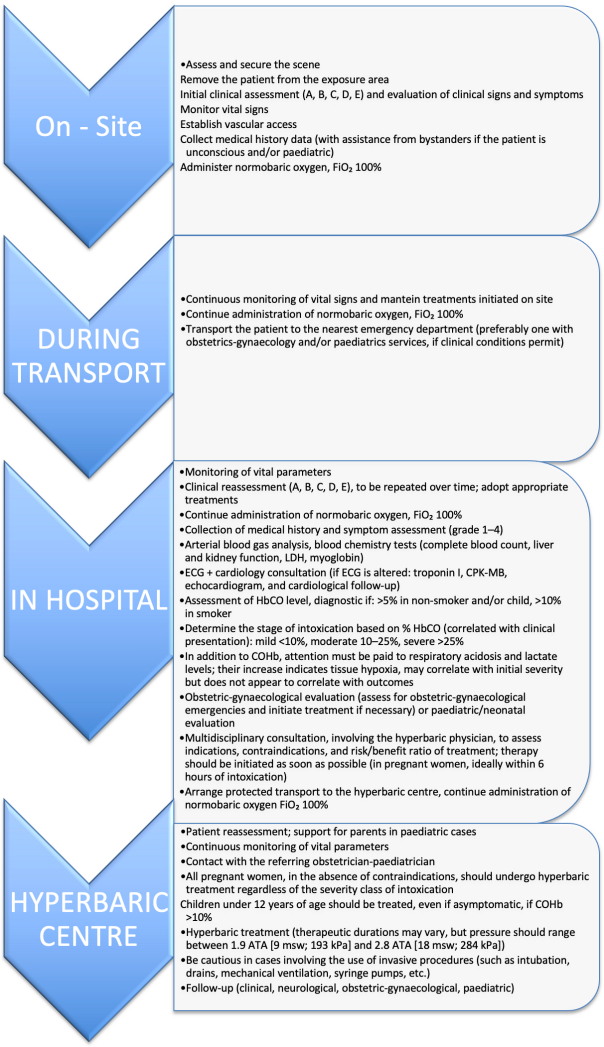

Figure 1. Clinical management algorithm.

Conclusion

Management of carbon monoxide poisoning in pregnant women and paediatric patients should be initiated as early as possible. A multidisciplinary approach is essential to optimise outcomes. The adoption of internal protocols—and ideally, the development of dedicated national guidelines—remains a priority.

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