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Neurological Effects of Acute Carbon Monoxide Poisoning in Children

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REVIEW ARTICLE

Neurological Effects of Acute Carbon Monoxide (CO) Poisoning in Children

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***Abstract**: Carbon monoxide poisoning (COP) is one of the most common causes of mortality and morbidity due to poisoning in all over the world. Although the incidence of COP has not been known exactly in the childhood, almost one-third of CO exposures occurred in children. The data regarding COP in children are inconclusive. Children may be more vulnerable to CO exposure than adults as a result of their high respiration and metabolic rates, high oxygen metabolism, and immature central nervous system. Recent researches proposed new theories about neurological effects of CO toxicity. The clinical presentations associated acute COP may be various and nonspecific. Unrecognized CO exposure may lead to significant morbidity and mortality. CO exposed children often become symptomatic earlier, and recover more rapidly, than similarly CO exposed adults. Mild clinical signs and symptoms associated with COP are headache, dizziness, weakness, lethargy, and myalgia; however, severe signs and symptoms such as blurred vision, syncope, convulsion, coma, cardiopulmonary arrest and death can also accompany with COP. Neurologic manifestations can include altered mental status at different degrees, neck stiffness, tremor, ataxia, and positive Babinski's sign. Delayed neurologic sequels (DNS) of COP might be seen in children like adults. DNS symptoms and signs in children include memory problems, mental retardation, mutism,* fecal and urinary incontinence, motor deficits, facial palsy, psychosis, chronic headache, seizures, and epilepsy. *After CO exposure children must be cared to detect and treat DNS. Although hyperbaric oxygen therapy (HBOT) is reported to prevent development of DNS, its indications, application duration and procedures are controversial in both of the children and adults. Although* their predictive values are limited, exposing to CO more than eight hours and suffering from CO-induced coma, *cardiac arrest, lactic acidosis, high COHb levels, and pathologic findings at* neuroimaging are reported to increase the risk factor for developing DNS. Since physiological properties of children are unique, clinical and experimental studies must be done to provide new perspectives in order to prevent or reduce both acute and delayed neurological effects of CO toxicity.

***Key words**: Acute carbon monoxide poisoning, carbon monoxide toxicity, children, hyperbaric oxygen therapy, neurological effects, delayed neurologic sequelae*
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Introduction

Carbon monoxide poisoning (COP) is one of the most common causes of mortality and morbidity due to poisoning in Turkey and all over the world [1-4]. The frequency of COP has been reported between 3.6–13.2% among childhood poisonings and between 58.2-75% among fatal childhood poisonings [4-6]. The major sources of carbon monoxide (CO) are faulty furnaces, inadequate ventilation of heating sources, and exposure to engine exhaust gases [7-8]. Children may be more vulnerable to CO exposure than adults as a result of their high respiration and metabolic rates, high oxygen metabolism, and immature central nervous system [9-10].

Pathophysiology of COP

The exact pathophysiology of CO toxicity is unclear. There are some different proposed mechanisms. When CO binds to hemoglobin decreases its oxygen transport capacity, also binding to myoglobin decreases its oxygen storage capacity and binding to mitochondrial cytochrome oxidase inhibits cellular respiration, with increased lipid peroxidation it causes harmful effects to CNS. [11-13] **(Figure 1)**. Also, excitotoxicity, increased atherogenesis, involvement with cytochrome p450, apoptosis, activation of hypoxia-inducible factor 1α (HIF-1α), and HIF-1α mediated gene regulation are other potential mechanism of CO toxicity [8,11]. HIF-1α regulates expression of genes involved in inflammation, metabolism, and cell survival, HIF-1α induced gene regulation can be protective or hazardous, depending on host factors [8,14]. It is shown that COP particularly affects iron rich regions of brain such as globus pallidus and substantia nigra (pars reticulata) and other parts of the brain, e.g., basal ganglia, central white matter, and hippocampus [11-13].

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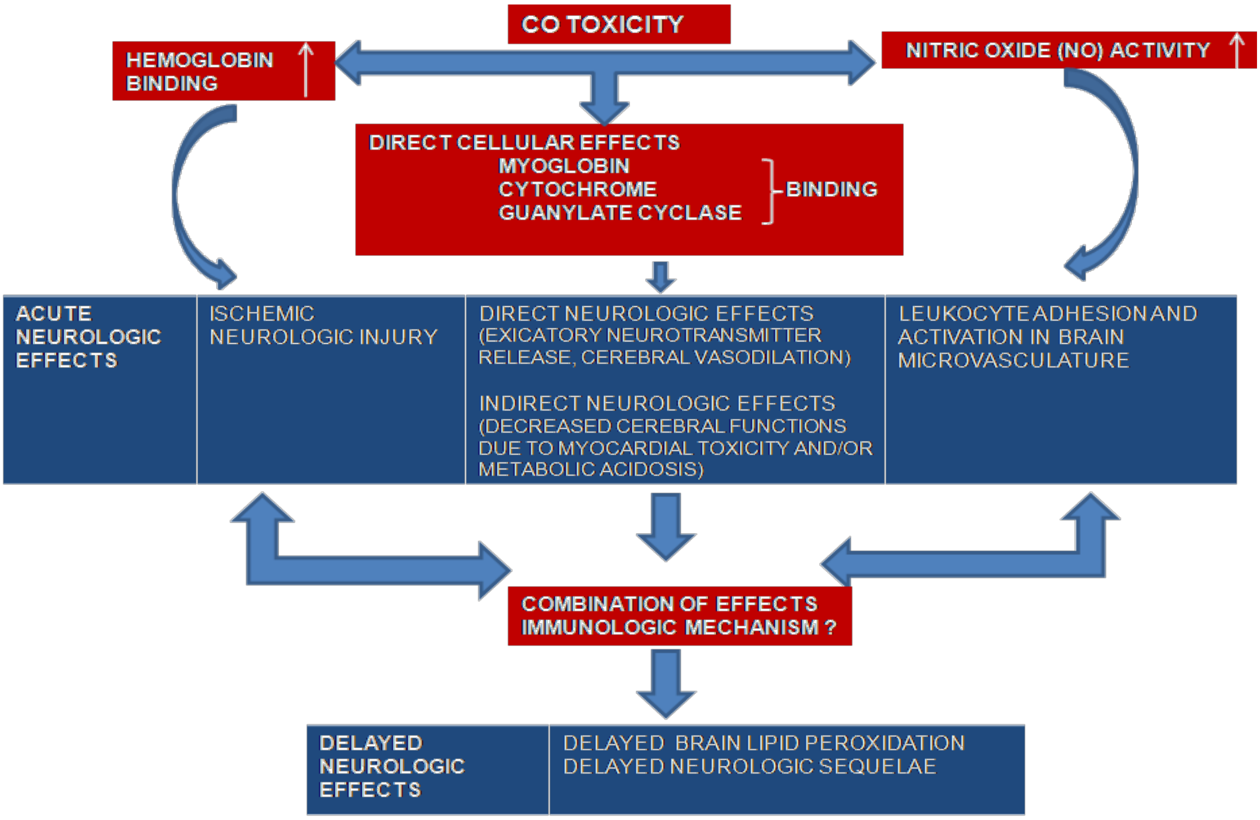

Figure 1. Proposed mechanisms involving in the pathophysiology of COP (adapted from ref. 11)

Clinical findings

The clinical presentations of COP may be various and nonspecific. Clinic symptoms are closely related to CO concentration in inhaled air and exposure time to CO. COHb levels may not correlate well with clinical findings at all times [11]. CO exposed children often become symptomatic earlier, and recover more rapidly, than similarly CO exposed adults [8]. Mild clinical signs and symptoms associated with COP are headache, dizziness, weakness, lethargy, and myalgia; however, severe signs and symptoms such as blurred vision, syncope, convulsion, coma, cardiopulmonary arrest and death can also accompany with COP [4,12,15,16]. Neurologic manifestations can include altered mental status at different degrees, neck stiffness, tremor, ataxia, and positive Babinski's sign [4,16]. Unrecognized CO exposure may lead to significant morbidity and mortality. Our previous research showed that the COHb levels of some of the asymptomatic children were found increased with history of CO exposure [4]. In the same study, the patients presented with neurological signs were found to have higher COHb blood levels and longer hospital stay [4]. Chronic COP can occur in poorly ventilated houses or living areas with faulty heating systems and can lead to headache, drowsing, and hyperactivity sign [17].

Delayed neurologic sequelae

Delayed neurologic sequelae (DNS) is shown to develop in 2.8-10.7% of children diagnosed with acute COP in 2 to 51 days after the poisoning [4,16,18,19]. DNS symptoms and signs in children include memory problems, mental retardation, mutism, fecal and urinary incontinence, motor deficits, facial palsy, psychosis, chronic headache, seizures, and epilepsy [4,16,18,19].

Laboratory findings

Blood COHb levels should be measured as soon as possible in CO exposed cases. In acute COP, central nervous system and cardiovascular system are primarily affected. Electrocardiography, cardiac enzymes and markers may be useful for detecting cardiovascular system insult. Neuroimaging may be used to rule out other conditions that might result changes in mental status.. Diffused brain edema, hypodense areas; particularly in globus pallidus, basal ganglia, and watershed areas; and rarely hydrocephaly can be seen at computed brain tomography [4,16,20]. Moreover, increased signals are reported in basal ganglia and white matter at T2-weighted brain MRI scans [12]. Neuropsychometric tests can use to assess and follow the cognitive functions in COP, but there are some restrictions for the using of these tests in children [11].

Diagnosis of COP

Suspecting from COP based on clinical symptoms and signs are critical for the diagnosis. In patient history, the presence of exposing to natural gas leakage and smoke, using water heater in poorly ventilated places, and sharing the same place with other CO poisoned persons are notable clues for the diagnosis of COP. Serum COHb levels should be obtained from patients suspected of CO exposure. A nonsmoker would be expected to have a baseline level less than 0.5% to 3%, whereas smokers may have levels as high as 4-10% [11,21]. The level of COHb can also increase in severe hemolytic anemia and sepsis (endogenous production). Detection of increased level of COHb in blood gas analysis is meaningful for the diagnosis; while lower level does not rule out it. Some factors might cause diagnostic difficulty such as delayed measurement of COHb level or oxygen therapy during transport [22].

Treatment of COP

Firstly, the patient should be quickly removed from the CO exposure area. ABC (Air Breathe and Circulation) of emergency management should immediately be established. Normobaric oxygen therapy should be administered through a nonrebreather reservoir face mask supplied with high flow oxygen, or 100% oxygen using artificial airway, if required, until the COHb level is less than 5% [8].

Hyperbaric oxygen therapy

Hyperbaric oxygen therapy (HBOT) is defined as the breathing of 100% oxygen by patients within hyperbaric chambers compressed to greater than normal atmospheric pressures [8]. The half life of COHb is 5 hours at room air (21% oxygen), 90 minutes at 100% oxygen, and 15 to 30 minutes at 100% HBOT at 3.0 atmosphere absolute (ATA) [23]. Although HBOT is reported to prevent development of DNS, its indications, application duration and procedures are controversial in both children and adults. Presence of few HBOT clinics, difficulties in transferring critically ill patients to these clinics restrict HBOT therapy in our country. Table I shows the recommended indications for HBOT in children [9,10,23,24].

HBOT is reported to be more effective if administered within 4-6 hours of COP [9] and repeated 3 times within 24 hours [25]. Moreover, HBOT may be effective in CO-induced brain injury as if it is given in one month after COP [21]. Besides its benefits in the treatment of COP, HBOT is not totally non-hazardous. HBOT can cause ear pain, convulsion, pulmonary edema and hemorrhage, and decompression sickness [4,26]; its use in pneumothorax is contraindicated [26].

Table I. Recommended Indications of HBOT in COP

- COHb level on blood gas analysis (arterial or venous) ≥ 25%
- Any loss of consciousness regardless of COHb level
- Any neurologic impairment regardless of COHb level
- Infants under six months of age with symptoms of lethargy, irritability, and poor feeding
- For pregnant patients, COHb level ≥ 15% or distress on fetal monitoring
- Presence of arrhythmia, anginal pain, or ischemic changes on an electrocardiogram
- Preexisting cardiovascular compromise with a COHb level greater than 20%

Prognosis of COP

The data regarding prognosis in children with COP are inconclusive. Exposing to CO more than eight hours and suffering from CO-induced coma, cardiac arrest, lactic acidosis, high COHb levels, and pathologic findings at neuro-imaging are reported to increase the risk factor for developing DNS. However their predictive values are limited [4,15,16,27].

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