Burning Down the House: Smoke Inhalation, Cyanide Toxicity, and Carbon Monoxide Poisoning

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Course Description:

They’re out of the burning house, now what? Smoke inhalation, cyanide (CN) toxicity and carbon monoxide (CO) poisoning are all important considerations in the patient with fire and smoke exposure. The emergency physician must be skilled in the identification and diagnosis of both CO and CN exposure, and must also be familiar with current treatment recommendations. Some of these therapies are new and some are controversial. This presentation will describe the pathophysiology and clinical presentation of patients with CN and CO exposure. New therapies such as hydroxocobalamin will be discussed with an emphasis on the literature and a comparison with “older” standard therapies. The controversial therapy of hyperbaric oxygen will also be discussed, considering the evidence for and against its use and for what specific indications.

Course Outline:

I. Case:

A 40-year old male is pulled from enclosed fire. He is confused and agitated. Upon arrival in the emergency department, he is disoriented and in moderate distress. He is coughing up soot, and has difficulty breathing.

Initial vital signs: BP 90/60, HR 120, RR 30, O2 sat 95%
PE: Singed nasal hair, soot around mouth, burns to face, arms and back.

What are the immediate concerns?

Laboratory Data:

VBG: pH 6.8, pO2 = 75, Lactate = 16 mmol/L COHgb = 20%

What now?

II. The Constituents of Smoke and Detection
A. We have a tendency to focus on CO as the diagnosis in victims of smoke inhalation. In part, this is the result of easy detection methods for CO.

- Traditional CO-Oximetry: CO-Oximetry uses multiple wavelengths of light to detect oxyhemoglobin, deoxyhemoglobin and carboxyhemaglobin species. Either a VBG or ABG must be drawn from the patients and sent to the laboratory for analysis.

- Non invasive CO-Oximetry: In 2005, the FDA approved a commercially available non invasive CO-Oximeter. The advantages of such a devise include more rapid diagnosis of a potentially life threatening condition and the ability to rapidly screen large numbers of patients. The accuracy of this device has recently been called into question. A study by Touger et al. (1) showed that (using a cutoff of 15% CO_hgb) the device only had a sensitivity of 48% with a specificity of 99%, and could not be reliably used in excluded CO exposure.

B. Pitfall - CN exposure is frequently overlooked. Consider that CN can be produced from the combustion of paper, silk, wool, plastic, and cotton. The probability of CN exposure in fires is therefore high. In the figure below data is presented from three different historical fires in which both CO and CN levels were measured. In some instances the number of patients exposed to CN is greater than that of carbon monoxide.

- Whole blood cyanide levels: Cyanide levels can be obtained but results can take several days. Therefore, cyanide levels cannot be used to direct treatment in the acute setting.

- Surrogate markers:
  - A plasma lactate level > 10 mmol/L is suggestive of the diagnosis
  - A reduced arterial-venous oxygen saturation is also suggestive of the diagnosis
III. The Pathophysiology of CO and CN Toxicity

A. The exact mechanism by which CO exerts its toxic effects is not entirely known. Here is some of what we do know:

- CO binds to hemoglobin with anywhere from 200-250 times the affinity of oxygen. Therefore CO displaces oxygen from hemoglobin resulting in a functional anemia and decreased oxygen carrying capacity in the blood.

- CO shifts the oxygen hemoglobin dissociation curve to the left. This results in a decreased ability of hemoglobin to deliver oxygen to the tissue as depicted in the following illustration (figure).

- CO is also known to bind to myoglobin, and may also cause the induction of lipid peroxidation. It is postulated that these mechanisms may be responsible for the persistent and delayed neurologic sequelae secondary to CO exposure, and for which the use of hyperbaric oxygen therapy has been suggested.

B. CN toxicity primary results from inhibition of the mitochondrial electron transport chain. It binds to cytochrome aa3 in the electron transport chain effectively shutting off oxidative phosphorylation and ATP production. (See illustration below). This results in the development of a severe elevated anion gap lactic acidosis.
IV. The Clinical Syndromes of CO and CN Poisoning

Carbon Monoxide

A. Acute poisoning

Can present as a spectrum from mild to severe. Mild exposure may mimic the flu with a presentation of headache, dizziness and generalized malaise. Symptoms resolve when the patient is removed from the source of the exposure. In severe poisoning, there is end organ damage secondary to acute hypoxemia and decreased delivery of oxygen to tissues including the brain, heart and other organs. Patient may present with seizures, coma, myocardial infarction, shock and multi-organ dysfunction.

B. Persistent neurologic sequelae

While there are no established diagnostic criteria, survivors of CO poisoning describe symptoms which persist from the time of poisoning. These include: Memory loss, impairments of concentration or language, affective changes such as depression and parkinsonism (2).

C. Delayed neurologic sequelae (DNS)

In some instances there is a latent period prior to the development of the above described symptoms. In this case the clinical syndrome is described as delayed neurologic sequelae. ²
Cyanide

A. Acute Poisoning

Patients typically present with signs and symptoms of cellular hypoxia including acidosis leading to nonspecific symptoms of headache, agitation and altered mental status. Symptoms typically progress to cardiovascular collapse with shock, respiratory arrest and rapid death.

B. Long term effects

Long term effects are not frequently addressed, but cyanide can contribute to significant morbidity (3). Cellular hypoxia can lead to lipid membrane peroxidation. Effects may be similar to the persistent and delayed neurologic sequelae of carbon monoxide exposure. Little is known about prevention of long-term effects from cyanide exposure.

V. Standard vs. New Therapies

A. The cyanide antidote kit

- Sodium Thiosulfate: Acts as a sulfur donor to enhance the endogenous elimination of CN through the rhodenase pathway.

- Sodium Nitrite and Amyl Nitrite: Both act to Induce methemoglobinemia (Methgb). Methgb does not bind CN with high affinity and therefore less CN is transported to the tissue. The downside is that both antidotes can cause significant hypotension and both further diminish the oxygen carrying capacity of hemoglobin.

B. Hydroxocobalamin

A natural form of vitamin B12, hydroxocobalamin detoxifies cyanide through the irreversible formation of cyanocobalamin, which is subsequently excreted in the urine. It essentially chelates CN. Its effectiveness has been demonstrated in multiple animal studies (4,5). A Prospective noncomparative trial in fire-smoke inhalation victims demonstrated survival of 72% in patients receiving Hydroxocobalamin (6).

C. Which antidotes should we use in the smoke inhalation victim?

Because of their ability to cause hypotension and to diminish the oxygen carrying capacity of hemoglobin both sodium nitrite and amyl nitrite should be avoided in the undifferentiated smoke inhalation victim. Sodium thiosulfate and hydroxocobalamin are considered safe. There are no head to head trials comparing these two antidotes.
VI. Controversies in Treatment: Hyperbaric Oxygen Therapy

A. The rationale for HBO therapy:

The rationale for hyperbaric oxygen (HBO) therapy stems from its ability to increase the elimination of CO (by shortening its half life), improving oxygenation (by increasing the amount of dissolved oxygen in the blood) and improving mitochondrial function and altering the inflammatory response secondary to CO poisoning.

B. How is HBO therapy performed?

C. Should we use HBO and if so what are the indications?

There is no clear answer to this question and therefore there is no standard of care. Review of the literature reveals 6 published studies relating to this question, 4 of which satisfied the criteria for inclusion in the most recent ACEP policy statement concerning this question (7-11). All of the studies evaluated the outcome of HBO therapy on neurologic outcome, but no other forms of morbidity related to CO poisoning or mortality. The body of literature suffers from several clear limitations:

- Lack of strict blinding of study participants and investigators
- Lack of objective and uniform assessment of outcomes
- Lack of rigorous quantification of the severity of any impairments
- Lack of structured assessment on the impact of therapy on quality of life
- Lack of any analysis of predefined subgroups to determine which patients might benefit from therapy

Experts most commonly identify loss of consciousness, persistent mental status alteration, pregnancy, and high carboxyhemoglobin levels as indications for HBO therapy. Until more evidence is provided, practitioners should consult their local poison control centers and experts for advice on a case by case basis, taking into consideration the availability of HBO and the severity of the patients clinical condition.

VII. Summary

- Smoke inhalation is responsible for more fire related deaths than burns.
- All smoke inhalation victims need rapid assessment of the ABCs, a complete trauma assessment, and finally evaluation for exposure to both CO and CN.
- Physicians tend to focus on CO exposure because of rapidly available CO level measurements.
- A significant number of fire victims will also have exposure to CN.
- Sodium nitrite and amyl nitrite should be avoided in the undifferentiated smoke inhalation patient.
- Hydroxocobalamin is an alternative antidote to the cyanide antidote kit for acutely poisoned patient. There are no head to head trials comparing hydroxocobalamin with sodium thiosulfate.
HBO therapy for acute CO exposure remains controversial. No definitive standard of care can be established based on the current literature.

References: