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Management of Co-Intoxications in the ICU Patient

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Stem Case and Key Questions Content

A 22 year- old male with a history of multiple suicide attempts is brought to the ED after being found unresponsive in a closed garage with an empty container of antifreeze near him. He is lethargic with respirations which are rapid and shallow. Heart rate is 100 bpm, blood pressure is 142/74, temperature is 38° Celsius, and the pulse oximeter reading is 100%. The ED physician requests assistance in evaluating the patient before administering sedation for a CT scan of the head.

Should this patient be intubated?
The ED physician insists that this patient does not require tracheal intubation since the pulse oximeter is consistently reading 100%.
Is the pulse oximeter reading of 100% reliable? Is there a better monitor to assess hemoglobin oxygen saturation?
Is there any additional clinical information that would help guide diagnosis/therapy at this point?
An artificial airway is secured at this time and the patient is administered 1.0 FiO2. Pulse oximeter reading remains steady at 100%.
Are there any further laboratory investigations that should be ordered at this time?
An arterial blood gas drawn immediately prior to intubation now is available and reveals the following: 7.12/28/61
What is the interpretation of this arterial blood gas?

What is the differential diagnosis at this time?
Distinguish between hypoxemia and hypoxia in this patient.
Are there any other laboratory values that would have been useful from this arterial sample?
Mechanical ventilation is instituted with the following parameters:
SIMV: RR 12 PEEP 5 cm H20
TV 800 mL Pressure Support 5 cm H20
Another arterial blood gas is drawn with the following results: 7.08/35/63. Additional parameters obtained from this sample include HbO2 saturation of 66% (pulse oximetry reading still 100%) and COHb saturation of 30%.
The diagnosis of carbon monoxide poisoning is made. The patient is treated with FiO2 1.0, and pO2 rises to 97 mmHg, but a metabolic acidosis persists.
What are the possible causes of the metabolic acidosis in this patient?
Based on history, the diagnosis of concurrent ethylene glycol poisoning is made. The patient is transferred to the ICU on full mechanical ventilatory support, and FiO2 remains at 1.0. In the

ICU, the patient's carboxyhemoglobin saturation level is noted to decrease (COHb 18%), but the patient has become even more acidemic (pH 7.01) and begins to develop multi-system organ failure, with acute renal failure and worsening neurologic status.
What is the difference between acidosis and academia?
What is the pathophysiology of a non-ethanol alcohol poisoning?
What are common types of alcohols seen in such poisonings?
What is the mechanism of end-organ failure?
What antidotes are available for these poisonings?
The appropriate antidote for ethylene glycol poisoning is administered but the patient's clinical and laboratory status continues to worsen. After renal replacement therapy is initiated, the patient does begin to improve.
What is the role of renal replacement therapy (RRT) in non-ethanol alcohol intoxications?
What are the possible long-term sequelae of these specific intoxications?

Model Discussion Content
The indications for an artificial airway include the need for ventilation, airway obstruction, and bronchial hygiene. (1) Ventilatory failure can be divided into either acute ventilatory failure or impending ventilatory failure. Acute ventilatory failure is diagnosed by an arterial blood gas consistent with a respiratory acidosis. Impending ventilatory failure is a clinical diagnosis in which exam findings may include use of accessory muscles and a subjective feeling of difficulty breathing. In a patient with rapid and shallow respirations, one would have to determine if this respiratory pattern is causing an increased work of breathing which would lead to respiratory muscle fatigue. Before making the decision regarding the need for sedation or intubation, the anesthesiologist should go to the bedside and evaluate the patient' work of breathing. Delivery of high concentrations of oxygen is not classically thought of as indication for placement of an artificial airway, since there are noninvasive systems capable of oxygen delivery at higher concentrations. One could argue that a patient who may require high levels of positive end expiratory pressure (PEEP) would require an artificial airway to deliver these pressures. In this patient, the altered mental status on arrival to the ED would be an indication for placement of an artificial airway. The altered mental status, with the lack of any obvious traumatic injury or known medical conditions, would also lead one to suspect the possibility of an overdose, intoxication, or poisoning. In order to help make the diagnosis of intoxication or poisoning, the history is clearly important, and the presence of certain toxidromes in the physical exam can be helpful. Not all intoxications or poisonings, however, have classic toxidromes with which they are associated, leading the clinician to rely solely on the history, subtle physical findings, and laboratory values. In this case, the history points to a differential diagnosis which must include carbon monoxide poisoning with likely concurrent ethylene glycol poisoning.

The arterial blood gas prior to intubation is consistent with a metabolic acidosis and hypoxemia. Hypoxemia is determined by an abnormally low concentration of dissolved oxygen in the blood. This is different than hypoxia. Hypoxia results from an inadequate oxygen delivery to tissues. In this patient, he is hypoxemic by the PaO2 of 61 mm HG on his arterial blood gas. He also may be hypoxic if his metabolic acidosis is from the accumulation of lactic acid from inadequate oxygen delivery to his tissues. Additional history and lactic levels should be attained at this time. Carbon monoxide poisoning is one of the most common fatal overdoses in the United States annually. (2,3,4) Carbon monoxide is an odorless, non-irritating gas produced by the combustion of a fuel source. The patient intoxicated with carbon monoxide may present with a

history of exposure to the byproducts of combustion in a closed non-ventilated space, such as a garage. (2,3) Common sources of carbon monoxide include automobile and gas stove exhaust. There is no classical toxidrome associated with carbon monoxide poisoning; most patients present with non-specific findings, such as tachycardia and tachypnea. The physical exam finding of “cherry reds lips” is classically associated with carbon monoxide poisoning.
Carbon monoxide causes cellular hypoxia by two mechanisms. First, it is a competitive inhibitor of oxygen with an affinity for hemoglobin greater than 200 times that of oxygen. This increased affinity causes the formation of carboxyhemoglobin. An increase in carboxyhemoglobin leads to decreased oxygen-carrying capacity within the blood, resulting in tissue hypoxia. The second mechanism of cellular hypoxia is related to a leftward shift of the oxygen disassociation curve in the presence of significant carboxyhemoglobinemia. This prevents unloading of oxygen molecules at the tissue level, causing cellular hypoxia.

Traditional pulse oximetry emits light at two wavelengths, one red and one blue. Absorption of oxygenated and deoxygenated blood at these two wavelengths during pulsatile flow is used to calculate a ratio which represents the oxyhemoglobin saturation. Because the red light absorption is nearly identical for both carboxyhemoglobin and oxyhemoglobin, the pulse oximeter cannot distinguish between these two hemoglobin moieties leading to an overestimation of the oxygen saturation when carboxyhemoglobin is present, making pulse oximetry unreliable in this setting. When carbon monoxide poisoning is suspected, an arterial blood sample should be obtained and measured by a co-oximeter, which will determine the amount of carboxyhemoglobin present. Co-oximeters use either four or eight wavelengths of light to distinguish multiple types of hemoglobins including carboxyhemoglobins. More recently, non-invasive pulse co-oximeters have become available and offer an alternative to arterial blood measurement of carboxyhemoglobin levels. (5, 6)

Patients with a history of smoking or chronic exposure to automobile exhaust may have levels of carboxyhemoglobin of 5 to 10%; these are considered mild COHb levels. Acute intoxications from carbon monoxide usually result in carboxyhemoglobin levels greater the 10%. Carboxyhemoglobin levels between 10% and 30% can lead to symptoms such as headache, nausea, dyspnea, and altered mental status. Carboxyhemoglobin levels greater the 30% can lead to coma and death. Long-term sequelae of carbon monoxide poisoning include a continuum of neurologic changes ranging from short term memory loss to a persistent vegetative state.
The treatment of carbon monoxide poisoning is largely supportive and includes the administration of oxygen with a FiO2 of 1.0. Isobaric oxygen treatment decreases the half-life of carbon monoxide from 4-6 hours to approximately 90 minutes. In patients with severe carbon monoxide intoxication presenting with coma or carboxyhemoglobin levels greater than 40%, hyperbaric oxygen may be indicated. Administration of hyperbaric oxygen furthers decreases the half life of carbon monoxide and may decrease the long term neurologic complications of carbon monoxide poisoning. There are, however, no strict guidelines or recommendations as to which patients are suitable candidates for hyperbaric oxygen therapy. (2, 4) The risk-benefit ratio of administration of hyperbaric oxygen and the availability of a nearby facility should play a role in the decision as to whether a patient should be transported to such a center for hyperbaric oxygen therapy.

Similar to hypoxia and hypoxemia, acidosis and acidemia are two different states that are frequently mistakenly interchanged. Acidosis refers to an increased hydrogen concentration in

the blood while academia refers to low blood ph. This patient has an acidemia reflected by the low ph caused by an increased hydrogen concentration caused by an introduction of an acid into the physiologic system.

Goals of ventilatory support can be thought of in terms of maintaining CO2 and the patient's work of breathing. The term full ventilatory support refers to having the patient do all the work of breathing while maintaining eucapnia. Partial ventilatory support refers to a ventilatory strategy in which eucapnia is maintained but the patient contributes to work of breathing. A third strategy is total ventilatory support in which the ventilator does all the work of breathing but the goal is not eucapnia. A classic example of total ventilatory support is hyperventilation for intracranial hypertension with the ventilator performing all the work of breathing with the goal of hypcapnia. Ethylene glycol, methanol, and isopropyl alcohol intoxication are associated with significant morbidity and mortality. The toxic byproducts of these compounds can cause metabolic, cardiopulmonary, and neurologic derangements. Ethylene glycol is a sweet-tasting, odorless substance found in antifreeze solutions. Because of these properties it is frequently ingested either accidentally or intentionally. Ethylene glycol itself is relatively nontoxic. Similar to methanol and acethominophen, the toxicity of ethylene glycol results from its degradation into toxic metabolites. Ethylene glycol is metabolized in the liver by alcohol dehydrogenase and converted into glycolic acid. Glycolic acid is the primary cause of the metabolic acidosis traditionally associated with ethylene glycol poisoning. Glycolic acid is further metabolized into glyoxylic acid, and then into oxalic acid. Accumulation of oxalic acid crystals is a cause of tissue damage in ethylene glycol poisoning.

Ethylene glycol intoxication is characteristically divided into four stages:
- Stage 1 (0-48 hours post-ingestion): inebriation, headache, ataxia, and anion gap metabolic acidosis
- Stage 2 (48-72 hours post-ingestion): end-organ dysfunction (heart and lungs)
- Stage 3 (after 72 hours post-ingestion): end-organ dysfunction (acute tubular necrosis of kidneys)
- Stage 4: long-term neurologic sequelae

Treatment of ethylene glycol intoxication involves assessing first the need for an artificial airway and circulatory support. Decreasing gastric absorption of ethylene glycol with gastric lavage may be indicated if the ingestion is less than one hour old. The next step in treatment is to provide a competitive inhibitor for the enzyme alcohol dehydrogenase to prevent formation of the toxic metabolites mentioned above. Historically, ethanol was used to provide this inhibition. Because of the potential side effects of altered mental status, hypoglycemia, and pancreatitis, however, it is no longer the primary agent of choice. (8,9) Fomepizole is the first line agent for ethylene glycol poisoning, functioning as a competitive inhibitor for alcohol dehydrogenase. (8) Fomepizole has less and fewer adverse side effects than ethanol, and has been shown to be efficacious in decreasing mortality after ethylene glycol intoxication. Bradycardia has been associated with fomepizole administration, but the incidence of altered mental status is greatly diminished compared to ethanol therapy. (8)

Historically, hemodialysis was a mainstay of treatment for ethylene glycol intoxication, removing the parent compound and its metabolites from the circulation. Ethylene glycol is water soluble, has an appropriate molecular weight and volume of distribution for hemodialysis. (10).

Clearance rates are higher with hemodialysis than with continuous renal replacement therapy which is the reason, HD is preferred over CRRT. (10) The indications for hemodialysis in this setting were:

- Visual impairment
- Renal failure
- Pulmonary edema
- Refractory acidosis
- Ethylene glycol levels greater than 50 mg/dl

While the increased use of fomepizole has decreased the need for hemodialysis in patients with ethylene glycol poisoning, those patients with severe kidney injury may still benefit from renal replacement therapy.

Methanol and isopropyl alcohol are the other two non- ethanol alcohol intoxications that can be seen. Methanol is a colorless, odorless, highly volatile chemical found most commonly in windshield washer fluid. Intoxication can be achieved by ingesting, inhalation or dermal absorption. Similar to ethylene glycol, methanol is metabolized by alcohol dehydrogenase to a toxic metabolite, formic acid. Formic acid is responsible for the signs of methanol poisoning such as headache, inebriation, ataxia and visual disturbance. Administration of folinic acid provides the cofactor for elimination of formic acid. Isopropyl alcohol, found in hand sanitizers, is more potent than ethylene glycol and methanol. Unlike methanol and ethylene glycol, isopropyl alcohol intoxication is associated with osmolal gap but no acidosis. This is because isopropyl alcohol is a secondary alcohol which is metabolized to acetone, a member of the ketone family. Acetone does not have free proton to donate, so it will not contribute to an acidosis. Unlike ethylene glycol and methanol which are primary acids whore byproducts are broken down to further acids, ketone are not broken down to further acids. This explains the minimal acidosis seen in isopropyl alcohol poisoning. Hemodialysis is required to eliminate the toxic metabolite from the body to prevent end organ dysfunction. As a side note, a frequent cause of confusion is the non- acidosis seen with the ketone production in isopropyl alcohol intoxication in contrast to the metabolic acidosis seen with ketone production in diabetic ketoacidosis. The acidosis seen in ketoacidosis is produced by the ketone bodies acetoacetate and beta hydroxybutyrate which have protons to donate into the physiologic system to contribute to a metabolic acidosis. The acetone produced in both ketoacidosis and isopropyl alcohol poisoning does not have a fee proton to donate to contribute to the systemic acidosis.

As this case demonstrates, both carbon monoxide and ethylene glycol poisoning have the potential to result in significant neurological injury. This injury can range from short-term memory lost to persistent vegetative states. It is important for the clinician, both inside and outside of the ICU, to be aware of the clinical presentations of these intoxications, and to be familiar with the treatments available for these exposures, for the safety and optimal resuscitation of these patients.

References

1 BA, Kacmarek RM, Peruzzi WT, Hauptman D. (1991). Clinical Application of Respiratory Care 4th Edition. Chicago: Mosby Year Book.
2 Maclennan N, Heimbach, DM, Cullen BF. (Volume 89 (3)). Anesthesia for Major Thermal

Injury. Anesthesiology , 749-770.
3 Weaver LK. (2009;360(12)). Carbon Monxide Poisoning. New England Journal of Medicine , 1217-1225.
4 Ernst A, Zibrak JD. (1998:339). Carbon Monoxide Poisoning. New England Journal Of Medicine , 1603-1608. 5 Kealey, G. (2009;30(1)). Carbon MonoxideToxicity. Journal of Burn care and Research , 146-147.
5 Kealey, G. (2009;30(1)). Carbon MonoxideToxicity. Journal of Burn care and Research , 146-147.
6 Fidkowski CW, Fuzaylov G, Sheridan RL, Cote CJ. (2009 Vol 19 (1)). Inhalation Burn Injury in Children. Paediatric Anesthesia , 147-54. 7 Suner S, Partridge R, Sucov A, Valente J, Chee K, Hughes A, Jay G. (2008 Vol 34(4)). Non-Invasive Pulse CO-oximetry Screening in the Emergency Department Identifies Occult carbon Monoxide Toxicity. Journal of Emergency Medicine , 441-450.
7 Suner S, Partridge R, Sucov A, Valente J, Chee K, Hughes A, Jay G. (2008 Vol 34(4)). Non-Invasive Pulse CO-oximetry Screening in the Emergency Department Identifies Occult carbon Monoxide Toxicity. Journal of Emergency Medicine , 441-450.
8 Brent J. (2009;360(21)). Fomepizole for Ethylene Glycol and Methanol Poisoning. New england Journal of Medicine , 2216-2223.
9 Lepik KJ, Levy AR, Sobolev BG, Purssell RA, Dewitt CR, Erhardt GD, Kennedy JR, Daws DE, Brignall JL. (2009 Vol 53,(4)). Adverse Drug Events Associated with the Antidotes for Methanol and Ethylene Glycol poisoning: A Comparsion of Ethanol and Fomepizole. Annals of Emergency Medicine , 439-450.
10 Goodman JW, Goldfarb DS (2006 Vol 19,(5)) The Role of Continuous Renal replacement therapy in the Treatment of Poisoning. Seminars in Dialysis 402-407