

Sodium Thiosulfate or Hydroxocobalamin for the Empiric Treatment of Cyanide

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Introduction

- Cyanide (CN) poisoning occurs in the settings of suicide, homicide, chemical warfare, genocide, enclosed space fires
- CN binds to cytochrome oxidase and other enzymes, producing cellular hypoxia, which leads to CNS and cardiovascular dysfunction
- Empiric treatment based on clinical findings: hypotension, AMS, elevated lactate (>10 mmol/L), relatively normal oxygen sat



Introduction

- Antidotes include amyl nitrite, sodium nitrite, sodium thiosulfate, hydroxocobalamin, dicobalt EDTA, 4-dimethylaminophenol
 - Only Na thiosulfate and hydroxocobalamin suitable for empiric therapy
- Purpose: to evaluate and review literature on hydroxocobalamin and Na thiosulfate monotherapy



Efficacy of Hydroxocobalamin

- Directly binds CN to form cyanocobalamin, which is renally excreted
- In vitro, penetrates cells and acts intracellularly
- In animals, crosses blood brain barrier
- In dogs, increased BP and lead to survival without neurological sequelae



Efficacy of Hydroxocobalamin

- Human *studies* - smoke inhalation
 - 1 prospective: 69 patients (37 coma, 14 CPA) given 5-15 g IV \Rightarrow 72% survival
 - 1 retrospective: 101 patients (72 survival status known - 41.7% survived, 38 arrest - 21 return of BP, 12 unstable - 9 BP recovered in 30 min)
- Case series and reports: suggest efficacy



Safety of Hydroxocobalamin

- Reddish brown discoloration of skin, mucous membranes and urine lasting several days
 - May complicate burn evaluation
 - May interfere with colorimetric assays for liver enzymes, bilirubin, creatinine, CK, phosphorus, glucose, magnesium, iron



Safety of Hydroxocobalamin

- Allergic reactions
- Hypertension with reflex bradycardia (self-limited)
- Headache, chest pressure in normal volunteers



Efficacy of Sodium Thiosulfate

- Conversion of CN to thiocyanate through action of rhodanese
- Limited distribution to brain and limited penetration into mitochondria
- In rabbits, 7/10 died.
 - Given alone, actually decreased time to death in poisoned animals



Efficacy of Sodium Thiosulfate

- In rats: decreased blood CN, lactate, venous pO₂ - suggesting efficacy
- Humans
 - No studies
 - Case series and reports - associated with survival



Safety of Sodium Thiosulfate

- Dogs given very high doses (3000 mg/kg, as opposed to typical human dose of 180 mg/kg) developed metabolic acidosis, hypoxemia, hypernatremia, hypotension
- Normal human volunteers - nausea and vomiting



Hydroxocobalamin & Thiosulfate

- Concern for chemical interactions if these agents are administered together, so should be given through separate IV lines
- No comparative studies



Conclusion

- Evidence for both hydroxocobalamin and sodium thiosulfate monotherapy is incomplete
- “Hydroxocobalamin seems to be an appropriate antidote for the empiric treatment of smoke inhalation and other suspected cyanide poisoning for victims in the out-of-hospital setting.”



Conclusion

- “Sodium thiosulfate can also be administered in the out-of-hospital setting.”
- “The onset of antidotal action of sodium thiosulfate may be too slow for it to be the only cyanide antidote for emergency use.”
 - Check out correspondence: Kerns W, Beuhler MB, Tomaszewski C. Ann of Emerg Med. March 2008 51(3)

