TITLE: Hydroxocobalamin for Cyanide Poisoning in the Pre-Hospital Setting: A Review of the Comparative Clinical Effectiveness and Safety

DATE: 26 June 2012

CONTEXT AND POLICY ISSUES

Smoke inhalation from an enclosed-space fire is the most likely cause of cyanide poisoning encountered by emergency medical services and firefighters. Fire-related mortality is more commonly associated with smoke inhalation than burns. Smoke toxicity has become a concern as industrial products have changed to synthetic materials that ignite and burn faster than natural materials. Smoke comprises particulate matter, carbon dioxide, hydrogen sulfide and hydrogen cyanide. Nitrogen and carbon-containing synthetics release hydrogen cyanide under conditions of high temperature and low oxygen characteristic of closed-space fires. While colorless and odorless, both carbon monoxide (CO) and hydrogen cyanide (HCN) reduce cognitive function impairing escape and increasing the risk of thermal injury. People with inhaled cyanide poisoning may become faint or drowsy, or show signs of vertigo, shortness of breath, rapid or irregular heartbeat, tremors, convulsions, paralysis, coma, respiratory or cardiovascular collapse.

Pre-hospital management of acute cyanide poisoning involves administering 100% oxygen through a non-rebreather mask, stabilizing vital signs, correcting acidosis and administering a cyanide antidote. While the only cyanide antidote for smoke inhalation in the United States is a cyanide antidote kit (Lilly kit, Taylor kit, Pasadena kit) containing amyl nitrite, thiosulfate and sodium nitrite, it is not for pre-hospital use. The nitrites in the kit reduce the blood’s oxygen-carrying capacity by binding hemoglobin, forming methemoglobin that neutralizes cyanide. In people with smoke inhalation-associated cyanide poisoning, concurrent CO poisoning typically compromises the blood’s oxygen-carrying capacity. Further reducing capacity from antidote-induced methemoglobinemia could prove fatal. Hydroxocobalamin (Cyanokit™) has been available as a cyanide antidote in France for almost a decade. Hydroxocobalamin binds with cyanide to form cyanocobalamin (vitamin B12) that is excreted in urine. Administered in the pre-hospital setting, hydroxocobalamin could potentially reduce morbidity and mortality from smoke inhalation-associated cyanide poisoning. While Hydroxocobalamin is available in Canada the Lilly and Pasadena kits are not.

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This review summarizes the comparative clinical effectiveness and safety of pre-hospital hydroxocobalamin for smoke inhalation-associated cyanide poisoning.

**RESEARCH QUESTIONS**

1. What is the comparative clinical effectiveness of hydroxocobalamin versus amyl nitrate or sodium thiosulfate for the treatment of cyanide poisoning resulting from smoke inhalation in the pre-hospital setting?

2. What is the clinical evidence regarding safety of hydroxocobalamin for the treatment of cyanide poisoning for the treatment of cyanide poisoning resulting from smoke inhalation in the pre-hospital setting?

**KEY MESSAGE**

No evidence was found regarding the comparative clinical effectiveness and safety of hydroxocobalamin versus amyl nitrite, thiosulfate and sodium nitrite for pre-hospital treatment of smoke inhalation-associated cyanide poisoning.

**METHODS**

**Literature Search Strategy**

A limited literature search was conducted on key health technology assessment resources, including MEDLINE (1946-) with in-process records & daily updates via Ovid; EMBASE (1974-) with daily updates via Ovid; PubMed, The Cochrane Library (Issue 5, 2012), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI (Health Devices Gold), EuroScan, international health technology agencies, and a focused Internet search. The search was limited to English language articles published between January 1, 2002 and May 29, 2012. No filters were applied to limit the retrieval by study type.

**Selection Criteria and Methods**

One reviewer screened citations to identify health technology assessments, systematic reviews, meta-analyses, randomized and non-randomized studies regarding the comparative clinical effectiveness and safety of hydroxocobalamin for smoke inhalation induced cyanide poisoning. Potentially relevant articles were ordered based on titles and abstracts, where available. One reviewer considered full-text articles for inclusion according to the selection criteria listed in Table 1.

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<th>Table 1. Selection Criteria</th>
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<td>Population</td>
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Exclusion Criteria

Articles were excluded if they did not satisfy the selection criteria, if they had incomplete methods, were included in a selected systematic review, were narrative reviews or case reports.

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 305 citations. Upon screening titles and abstracts, eight potentially relevant articles were retrieved for full-text review. No further potentially relevant report were retrieved from grey literature or hand searching. Of the eight potentially relevant reports, six were nonsystematic reviews and two were non-comparative non-randomized studies. No relevant publications were included in this review. The process of study selection is outlined in the PRISMA flowchart (Appendix 1).

Comparative Clinical Effectiveness and Safety of Hydroxocobalamin for Cyanide Poisoning

No evidence was found regarding the clinical effectiveness and safety of hydroxocobalamin versus cyanide antidote kits containing amyl nitrite, thiosulfate and sodium nitrite for smoke inhalation-associated cyanide poisoning. The safety of pre-hospital hydroxocobalamin for cyanide poisoning was reported in two non-comparative studies found in Appendix 2.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No evidence was found regarding the comparative clinical effectiveness and safety of hydroxocobalamin versus amyl nitrite, thiosulfate and sodium nitrite for pre-hospital treatment of smoke inhalation-associated cyanide poisoning.

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References


APPENDIX 1: Selection of Included Studies

305 citations identified from electronic literature search and screened

→ 297 citations excluded

8 potentially relevant articles retrieved for scrutiny (full text, if available)

0 potentially relevant reports retrieved from other sources (grey literature, hand search)

8 potentially relevant reports

→ 8 reports excluded:
- no comparator (2)
- other (review articles, editorials) (6)

0 report included in review
APPENDIX 2: Additional Information (Non-comparative Studies)
