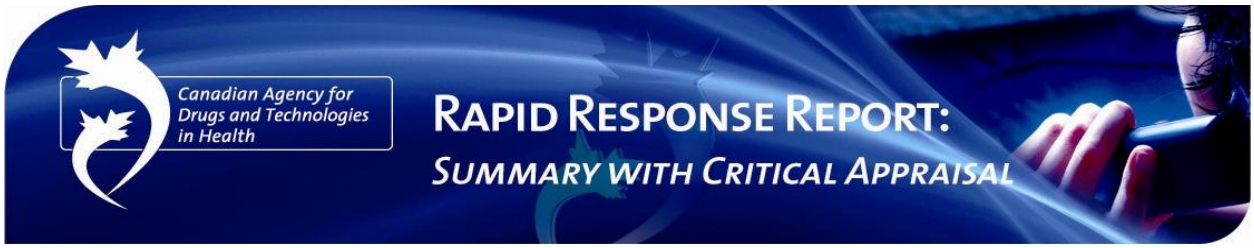


TITLE: Hydroxocobalamin for Cyanide Poisoning in the Pre-Hospital Setting: A Review of the Comparative Clinical Effectiveness and Safety

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.[1] 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.[1] 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.[1]

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.[1] 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.[1] Hydroxocobalamin (Cyanokit™) has been available as a cyanide antidote in France for almost a decade.[1] 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[2] and the Taylor kit[3] are available in Canada the Lilly and Pasadena kits are not.[3]

Disclaimer: The Rapid Response Service is an information service for those involved in planning and providing health care in Canada. Rapid responses are based on a limited literature search and are not comprehensive, systematic reviews. The intent is to provide a list of sources and a summary of the best evidence on the topic that CADTH could identify using all reasonable efforts within the time allowed. Rapid responses should be considered along with other types of information and health care considerations. The information included in this response is not intended to replace professional medical advice, nor should it be construed as a recommendation for or against the use of a particular health technology. Readers are also cautioned that a lack of good quality evidence does not necessarily mean a lack of effectiveness particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up to date, CADTH does not make any guarantee to that effect. CADTH is not liable for any loss or damages resulting from use of the information in the report.

Copyright: This report contains CADTH copyright material. It may be copied and used for non-commercial purposes, provided that attribution is given to CADTH.

Links: This report may contain links to other information available on the websites of third parties on the Internet. CADTH does not have control over the content of such sites. Use of third party sites is governed by the owners' own terms and conditions.

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.

Table 1. Selection Criteria

Population	Patients treated for cyanide poisoning (known or suspected) in the pre-hospital setting
Intervention	Hydroxocobalamin
Comparator	Amyl nitrate, sodium thiosulfate (eg Lilly kit, Pasadena kit)
Outcomes	Comparative clinical effectiveness, safety (patient and caregiver), ease of administration
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and non-randomized studies

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.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
Tel: 1-866-898-8439
www.cadth.ca

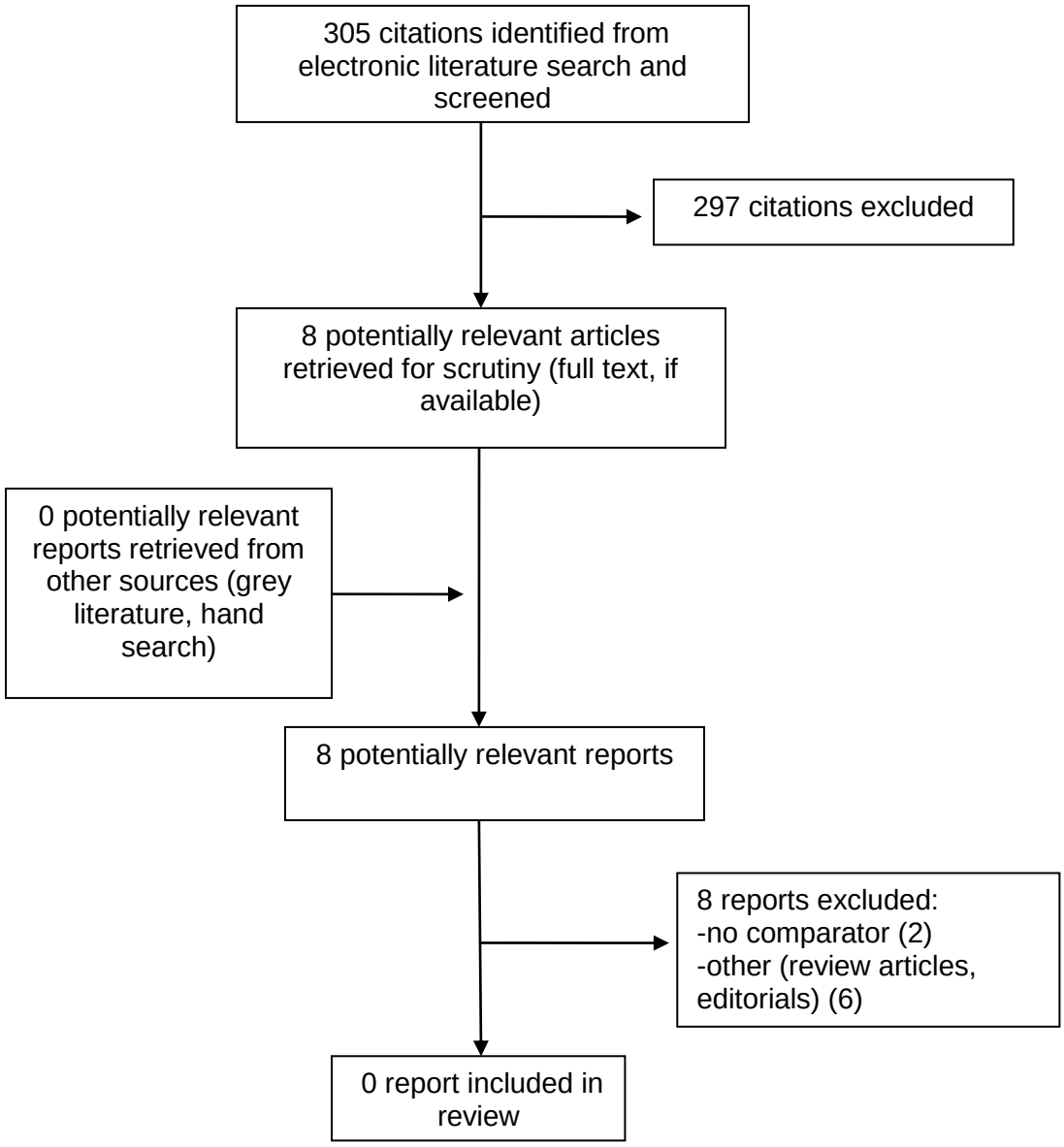
References

1. Smoke inhalation & hydrogen cyanide poisoning [Internet]. San Diego: Jems Communications; 2004. [cited 2012 Jun 19]. Available from: http://www.colofirechiefs.org/CSFCA%20Documents/smoke_poisoning.pdf

2. Cyanokit. 2010 Dec 17 [cited 2012 Jun 22]. In: Health Canada. Notice of Compliance (NOC) [Internet]. Ottawa: Health Canada; 1994 - . Available from: http://webprod3.hc-sc.gc.ca/noc-ac/newSearch-nouvelleRecherche.do?lang=eng DIN: 02360721.

3. Davis J. Toxicology of urgency: treatment of poisoning by cyanide [Internet]. Reno (NV): Oboulo.com Inc; 2009 May 18. [cited 2012 Jun 22]. Available from: http://en.oboulo.com/toxicology-of-urgency-treatment-of-poisoning-by-cyanide-64720.html

APPENDIX 1: Selection of Included Studies



APPENDIX 2: Additional Information (Non-comparative Studies)

4. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. Ann Emerg Med. 2007 Jun;49(6):794-801.
5. Fortin JL, Giocanti JP, Ruttimann M, Kowalski JJ. Prehospital administration of hydroxocobalamin for smoke inhalation-associated cyanide poisoning: 8 years of experience in the Paris Fire Brigade. Clin Toxicol (Phila). 2006;44 Suppl 1:37-44.