

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

Methoxyflurane for Acute Pain: Clinical Effectiveness

Service Line: Rapid Response Service
Version: 1.0
Publication Date: May 21, 2020
Report Length: 6 Pages

Authors: Christopher Freige, Charlene Argáez

Cite As: Methoxyflurane for acute pain: clinical effectiveness. Ottawa: CADTH; 2020 May. (CADTH rapid response report: reference list).

Disclaimer: The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to requests@cadth.ca

Research Questions

1. What is the comparative clinical effectiveness of methoxyflurane versus inhaled nitrous oxide for acute pain?
2. What is the clinical effectiveness of methoxyflurane for acute pain in pre-hospital or emergency department settings?

Key Findings

One systematic review was identified regarding the comparative clinical effectiveness of methoxyflurane versus inhaled nitrous oxide for acute pain in the emergency setting.

Methods

A limited literature search was conducted by an information specialist on key resources including OVID Medline/EMBASE databases. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine’s MeSH (Medical Subject Headings), and keywords. The main search concepts were methoxyflurane and nitrous oxide and pre-hospital setting. No search filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2018 and May 13, 2020. Internet links are provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Populations	Q1: Adult patients (i.e., age 18 or older) with acute pain in any setting Q2: Adult patients (i.e., age 18 or older) with acute pain in pre-hospital or emergency department settings
Intervention	Low-dose, inhaled methoxyflurane (e.g., Pentrox)
Comparators	Q1: Inhaled nitrous oxide (i.e., ready-to-use gas mixture of 50% nitrous oxide and 50% oxygen [e.g., Entonox]) Q2: Inhaled, oral, intranasal, or atomized analgesics
Outcomes	Clinical effectiveness (e.g., pain relief, need for other analgesics) or harm (e.g., nausea, dizziness, abdominal distension)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Results

One systematic review¹ was identified regarding the comparative clinical effectiveness of methoxyflurane versus inhaled nitrous oxide for acute pain in the emergency setting. No health technology assessments, randomized controlled trials, or non-randomized studies were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

1. Porter KM, Siddiqui MK, Sharma I, Dickerson S, Eberhardt A. Management of trauma pain in the emergency setting: low-dose methoxyflurane or nitrous oxide? A systematic review and indirect treatment comparison. *J Pain Res.* 2018;11:11-21.
[PubMed: PM29302193](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Appendix — Further Information

Previous CADTH Reports

2. Wells C, Adcock L. Methoxyflurane for acute pain in the emergency department: a review of clinical effectiveness, cost-effectiveness and guidelines [CADTH rapid response report: summary with critical appraisal]. Ottawa (ON): CADTH; 2018 Aug: <https://cadth.ca/sites/default/files/pdf/htis/2018/RC1006%20Methoxyflurane%20for%20Acute%20Pain%20Final.pdf> Accessed 2020 May 20.
3. Yeung SST, Adcock L. Methoxyflurane in pre-hospital settings: a review of clinical effectiveness, cost-effectiveness and guidelines [CADTH rapid response report: summary with critical appraisal]. Ottawa (ON): CADTH; 2018 Nov: <https://cadth.ca/sites/default/files/pdf/htis/2018/RC1038%20Methoxyflurane%20in%20Pre-Hospital%20Settings%20Final.pdf> Accessed 2020 May 20.

Systematic Reviews and Meta-Analyses

Alternative Population

4. Hartshorn S, Middleton PM. Efficacy and safety of inhaled low-dose methoxyflurane for acute paediatric pain: a systematic review. *Trauma*. 2019 Apr;21(2):94-102; <https://journals.sagepub.com/doi/full/10.1177/1460408618798391> Accessed 2020 May 20.

Randomized Controlled Trials

Unclear Comparator

5. Borobia AM, Collado SG, Cardona CC, et al. Inhaled methoxyflurane provides greater analgesia and faster onset of action versus standard analgesia in patients with trauma pain: InMEDIATE: a randomized controlled trial in emergency departments. *Ann Emerg Med*. 2020 03;75(3):315-328. [PubMed: PM31623936](https://pubmed.ncbi.nlm.nih.gov/31623936/)
6. Young L, Bailey GP, McKinlay JAC. Service evaluation of methoxyflurane versus standard care for overall management of patients with pain due to injury. *Adv Ther*. 2020 May;37(5):2520-2527. [PubMed: PM32232663](https://pubmed.ncbi.nlm.nih.gov/32232663/)
7. Borobia Perez AM, Collado SG, Cardona CC, et al. Results of a phase IIIB, open label randomised clinical trial to compare pain relief between methoxyflurane and standard of care analgesia for treating patients with trauma pain in Spanish emergency departments. *Basic Clin Pharmacol Toxicol*. 2018 Sep;123 (Suppl 4):16; [http://www.ibjournals.com/IBJ-CP/articles/2017/v1/e0008/protocol-ABP-IBJCP-2017-1\(1\)e0008.pdf](http://www.ibjournals.com/IBJ-CP/articles/2017/v1/e0008/protocol-ABP-IBJCP-2017-1(1)e0008.pdf) Accessed 2020 May 20.

Alternative Comparator

8. Lim KJ, Koh ZX, Ng YY, et al. Comparison of inhalational methoxyflurane (Penthrox®) and intramuscular tramadol for prehospital analgesia. *Singapore Med J*. 2020 Mar. [PubMed: PM32179922](https://pubmed.ncbi.nlm.nih.gov/32179922/)

9. Ricard-Hibon A, Lecoules N, Savary D, et al. Inhaled methoxyflurane for the management of trauma related pain in patients admitted to hospital emergency departments: a randomised, double-blind placebo-controlled trial (PenASAP study). *Eur J Emerg Med.* 2020 Apr 08;08:08.
[PubMed: PM32282467](#)
10. Voza A, Ruggiano G, Serra S, et al. Inhaled Methoxyflurane versus intravenous morphine for severe trauma pain in the emergency setting: subgroup analysis of MEDITA, a multicenter, randomized, controlled, open-label trial. *J Pain Res.* 2020;13:491-502.
[PubMed: PM32184653](#)

Review Articles

Unclear Methodology – Methods may be systematic

11. Williams OD, Pluck G. The use of methoxyflurane (Pentrox) for procedural analgesia in the emergency department and pre-hospital environment. *Trauma.* 2020 Apr;22(2):85-93;
<https://journals.sagepub.com/doi/abs/10.1177/1460408619850038#abstract>
Accessed 2020 May.
12. Rahman SM, Quinn E. BET 1: Green or blue for you? Methoxyflurane (Pentrox) or nitrous oxide/oxygen 50% mixture (Entonox) for the management of acute pain in the ED. *Emerg Med J.* 2019;36(8):506-508.
[PubMed: PM31358553](#)