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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Intranasal Sufentanil for Acute Pain: Clinical Effectiveness and Guidelines

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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.

Research Questions

1. What is the clinical effectiveness of intranasal sufentanil for acute pain in adults?
2. What are the evidence-based guidelines regarding the use of intranasal opioids for acute pain in adults?

Key Findings

Three evidence-based guidelines were identified regarding the use of intranasal opioids for acute pain in adults.

Methods

A limited literature search was conducted on PubMed, EMBASE, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. For question #1, no methodological filters were applied to limit retrieval by study type. For question #2, methodological filters were applied to limit retrieval to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2012 and November 20, 2017. Internet links were 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

Population	Adult patients with acute pain
Interventions	Q1: Intranasal sufentanil Q2: Intranasal opioids (e.g., sufentanil, ketamine, or fentanyl)
Comparators	Q1: Standard of care (intravenous morphine, hydromorphone); Intranasal fentanyl; Ketamine Q2: No comparator
Outcomes	Q1: Clinical effectiveness (benefit/harm), safety, time to onset of pain relief Q2: Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Three evidence-based guidelines were identified regarding the use of intranasal opioids for acute pain in adults. No relevant health technology assessment, systematic reviews, meta-analyses, randomized controlled trials, or non-randomized studies were identified regarding the clinical effectiveness of intranasal sufentanil for acute pain in adults.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Three evidence-based guidelines[1-3] were identified regarding the use of intranasal (IN) opioids for acute pain in adults.

In terms of IN opioid use, the Intranasal Medication Administration guidelines by the Emergency Nurses Association recommend the use of IN fentanyl to treat moderate to severe pain in both adults and children (aged one to 18) in the emergency setting.[1] In addition, IN ketamine may be a safe and effective intervention for pain management in the emergency setting; however, there is insufficient evidence to recommend the use of IN sufentanil in the emergency setting.[1] Recommendations from the National Institute for Health and Care Excellence (NICE) guidelines regarding the assessment and initial management of major trauma include considering the IN route for the delivery of diamorphine or ketamine for pain relief in the pre-hospital and hospital setting if an intravenous (IV) line has not been established.[2] In terms of potential harms, NICE indicates that caution should be heeded when administering pain relief intranasally and then administering it intravenously due to the additive dosing effects.[2] In addition, IN administration is contraindicated in cases where there is facial trauma or severe head injury.[2] The NICE recommendations for the assessment and initial management of spinal injury include considering the IN administration route for the atomized delivery of diamorphine or ketamine for pain relief in the pre-hospital or hospital setting if an IV line has not been established.[3]

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Guidelines and Recommendations

1. Emergency Nurses Association. Clinical practice guideline: intranasal medication administration [Internet]. Des Plaines (IL): Emergency Nurses Association; 2016 [cited 2017 Nov 27]. Available from: https://www.ena.org/docs/default-source/resource-library/practice-resources/cpg/intranasalmedcpg.pdf?sfvrsn=c9522db_8

2. Guideline Summary: Major trauma: assessment and initial management. In: National Guideline Clearinghouse [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2016 [cited 2017 Nov 27].
   Summary available from: https://www.guideline.gov/summaries/summary/50078/major-trauma-assessment-and-initial-management?q=intranasal+opioid
   See: Pain Relief
   Potential Harms, bullet 12

3. Guideline summary: Spinal injury: assessment and initial management. In: National Guideline Clearinghouse [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2016 [cited 2017 Nov 27].
   Summary available from: https://www.guideline.gov/summaries/summary/50080/spinal-injury-assessment-and-initial-management?q=intranasal+opioid
   See: Pain Relief

Appendix — Further Information

Previous CADTH Reports

4. Sufentanil for palliative pain relief: a review of the clinical effectiveness, cost-effectiveness, and guidelines [Internet]. Ottawa (ON): CADTH; 2015 [cited 2017 Nov 27]. Available from: https://www.cadth.ca/sites/default/files/pdf/htis/nov-2015/RC0728%20Sufentanil%20Final.pdf

5. Intranasal versus intravenous administration of anxiolytic and analgesic medications: comparative clinical effectiveness [Internet]. Ottawa (ON): CADTH; 2014 [cited 2017 Nov 27].
Available from: https://www.cadth.ca/sites/default/files/pdf/htis/feb-2014/RB0641%20Intranasal%20Administration%20Final.pdf

6. Patient-controlled analgesia for acute injury transfers: a review of the clinical effectiveness, safety, and guidelines [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2014 Aug [cited 2017 Nov 27]. (CADTH Rapid Response Report: Summary with Critical Appraisal). Available from: https://www.ncbi.nlm.nih.gov/books/NBK254078/

7. Pain management for pediatric patients in the emergency department: guidelines [Internet]. Ottawa (ON): CADTH; 2013 [cited 2017 Nov 27].
Available from: https://www.cadth.ca/sites/default/files/pdf/htis/dec-2013/RA0652%20Pediatric%20Pain%20in%20ED%20final.pdf

Systematic Reviews and Meta-Analyses

Alternative Intervention

8. Hansen MS, Dahl JB. Limited evidence for intranasal fentanyl in the emergency department and the prehospital setting - a systematic review [Internet]. Danish Med J; 2013 [cited 2017 Nov 27]. 60(1):A4563.
Available from:
http://www.danmedj.dk/portal/page/portal/danmedj.dk/dmj_forside/PAST_ISSUE/2013/DMJ_2013_01/A4563

Alternative Intervention in Pediatric Population

9. Murphy A, O'Sullivan R, Wakai A, Grant TS, Barrett MJ, Cronin J, et al. Intranasal fentanyl for the management of acute pain in children [Internet]. Cochrane Database Sys Rev. 2014 Oct [cited 2017 Nov 27]. Available from:
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009942.pub2/full

Randomized Controlled Trials – Alternative Intervention

10. Yang L, Sun DF, Wu Y, Han J, Liu RC, Wang LJ. Intranasal administration of butorphanol benefits old patients undergoing H-uvulopalatopharyngoplasty: a randomized trial. BMC Anesthesiol. 2015 Feb 2;15:20. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4429317
PubMed: PM25972155

Non-Randomized Studies

No Comparator

11. Steenblik J, Goodman M, Davis V, Gee C, Hopkins CL, Stephen R, et al. Intranasal sufentanil for the treatment of acute pain in a winter resort clinic. Am J Emerg Med. 2012 Nov;30(9):1817-21.
PubMed: PM22633713

12. Stephen R, Lingenfelter E, Broadwater-Hollifield C, Madsen T. Intranasal sufentanil provides adequate analgesia for emergency department patients with extremity injuries. J Opioid Manag. 2012 Jul;8(4):237-41.
PubMed: PM22941851

Pediatric Population and Combined Intervention

13. Nielsen BN, Friis SM, Romsing J, Schmiegelow K, Anderson BJ, Ferreiros N, et al. Intranasal sufentanil/ketamine analgesia in children. Paediatr Anaesth. 2014 Feb;24(2):170-80.
PubMed: PM24118506

Alternative Intervention

14. Schacherer NM, Erikson RD, Frazier SB, Perkins AM. Expedited delivery of pain medication for long-bone fractures using an intranasal fentanyl clinical pathway. Pediatr Emerg Care. 2015 Aug;31(8):560-3.
PubMed: PM25875994

Guidelines and Recommendations – Pediatric Population

15. Guideline summary: Fractures (non-complex): assessment and management. In: National Guideline Clearinghouse [Internet]. Rockville (MD): Agency for Healthcare Research and Quality; 2016 [cited 2017 Nov 27].
Summary available from:
https://www.guideline.gov/summaries/summary/50077/fractures-noncomplex-assessment-and-management?q=intranasal+opioid
See: Initial Pharmacological Management of Pain in Children (Under 16s), second Bullet

Clinical Practice Guidelines – Uncertain Methodology

16. Scottish Palliative Care Guidelines: choosing and changing opioids [Internet]. Edinburgh, Scotland: NHS Scotland; 2017 [cited 2017 Nov 27].
Available from:
http://www.palliativecareguidelines.scot.nhs.uk/guidelines/pain/choosing-and-changing-opioids.aspx
See: Fentanyl sublingual/intranasal

17. Northwest Healthcare Response Network (Washington State). Intranasal (IN) medication administration: MBED clinical practice guideline [Internet]. Tukwila (WA): Northwest Healthcare Response Network; 2014 [cited 2017 Nov 27]. Available from:
http://www.nwhrn.org/media/No-Pain-Intranasal-Medication-Administration-MBED-Clinical-Practice-Guideline1.pdf

18. Providence HealthCare. Intranasal fentanyl protocol [Internet]. Vancouver (BC): St. Paul's Hospital Emergency Department; 2012 [cited 2017 Nov 27]. Available from: http://sphemerg.ca/wp-content/uploads/2016/09/Intranasal-Fentanyl-Protocol.pdf

Review Articles

19. Ziesenitz VC, Vaughns JD, Koch G, Mikus G, van den Anker JN. Pharmacokinetics of fentanyl and its derivatives in children: a comprehensive review. Clin Pharmacokinet. 2017 Jul 7.
PubMed: PM28688027

20. AlSarheed MA. Intranasal sedatives in pediatric dentistry. Saudi Med J. 2016 Sep;37(9):948-56. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5039613
PubMed: PM27570849

21. Corrigan M, Wilson SS, Hampton J. Safety and efficacy of intranasally administered medications in the emergency department and prehospital settings. Am J Health Syst Pharm. 2015 Sep 15;72(18):1544-54.
PubMed: PM26346210

22. Grassin-Delyle S, Buenestado A, Naline E, Faisy C, Blouquit-Laye S, Couderc L-J, et al. Intranasal drug delivery: An efficient and non-invasive route for systemic administration - Focus on opioids. Pharmacol Ther. 2012;134(3):366-79.
PubMed: PM22465159