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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Nonsteroidal Anti-Inflammatory Drugs for Chronic Pain in Pediatric Populations: Clinical Effectiveness

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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.

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Research Question

What is the clinical effectiveness of nonsteroidal anti-inflammatory drugs for the treatment of chronic pain in pediatric patients?

Key Findings

Five systematic reviews were identified regarding the clinical effectiveness of nonsteroidal anti-inflammatory drugs for the treatment of chronic pain in pediatric patients.

Methods

A limited literature search was conducted by an information specialist on key resources including Medline, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. 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 NSAIDs and chronic pain in the pediatric population. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between Jan 1, 2015 and Apr 16, 2020. 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	Pediatric patients with chronic pain, including pain from chronic daily headaches, migraines, back pain, abdominal pain, idiopathic local pain, chronic widespread pain and fibromyalgia, and complex regional pain syndrome
Intervention	Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen, naproxen, ketorolac)
Comparator	Other pharmacological medications (e.g., gabapentin, pregabalin, amitriptyline, nortriptyline, duloxetine, acetaminophen) Placebo Non-pharmacological interventions (e.g., physiotherapy, exercise, counseling, neurostimulation)

Outcomes	Clinical effectiveness (e.g., change in pain symptoms, change in quality of life, functional outcomes, disability)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

Results

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

Five systematic reviews[1-5] (one overview of systematic reviews[1] and another overview of systematic reviews with meta-analysis[5]) were identified regarding the clinical effectiveness of non-steroidal anti-inflammatory drugs for the treatment of chronic pain in pediatric patients. No relevant health technology assessments, randomized controlled trials, or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Five systematic reviews[1-5] (one overview of systematic reviews[1] and another overview of systematic reviews with meta-analysis[5]) were identified regarding the clinical effectiveness of nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of chronic pain in pediatric patients. The authors of the identified overview of systematic reviews[1] found no evidence from randomized controlled trials (RCTs) that NSAIDs, such as ibuprofen, were effective for chronic non-cancer pain in children and adolescents.[1] Consequently the authors of another systematic review[2] aimed to assess the analgesic efficacy, and adverse events, of NSAIDs used to treat cancer-related pain in children and adolescents and also found no evidence. The same authors conducted another systematic review[3] aimed at reviewing the efficacy and safety of utilizing NSAIDs to treat chronic non-cancer pain in children and adolescents and identified seven RCTs. However, the data was insufficient and the authors could not draw any conclusions about the efficacy or harm of NSAIDS on chronic non-cancer pain.[3] The authors of another systematic review[4] aimed to assess the effects of pharmacological interventions such as NSAIDs versus placebo for the treatment of migraines in children and adolescents. The authors identified two low quality trials, concluding that ibuprofen was more effective than placebo for relieving pain, while another trial found that sumatriptan plus naproxen sodium was also effective in treating adolescents with migraine.[4] The authors also made note that there was limited information available on adverse events related to ibuprofen use.[4] The last identified overview of systematic reviews with meta-analysis[5] concluded that ibuprofen at conventional doses was consistently superior to paracetamol at providing pain relief for a range of painful conditions including osteoarthritis, rheumatoid arthritis, migraines, and back pain.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Radman M, Babic A, Runjic E, et al. Revisiting established medicines: An overview of systematic reviews about ibuprofen and paracetamol for treating pain in children. *Eur J Pain*. 2019 Jul;23(6):1071-1082.
PubMed: PM30793444

2. Cooper TE, Heathcote LC, Anderson B, Gregoire MC, Ljungman G, Eccleston C. Non-steroidal anti-inflammatory drugs (NSAIDs) for cancer-related pain in children and adolescents. *Cochrane Database Syst Rev*. 2017 07 24;7:CD012563.
PubMed: PM28737843

3. Eccleston C, Cooper TE, Fisher E, Anderson B, Wilkinson NM. Non-steroidal anti-inflammatory drugs (NSAIDs) for chronic non-cancer pain in children and adolescents. *Cochrane Database Syst Rev*. 2017 08 02;8:CD012537.
PubMed: PM28770976

4. Richer L, Billinghurst L, Linsdell MA, et al. Drugs for the acute treatment of migraine in children and adolescents. *Cochrane Database Syst Rev*. 2016 Apr 19;4:CD005220.
PubMed: PM27091010

5. Moore RA, Derry S, Wiffen PJ, Straube S, Aldington DJ. Overview review: Comparative efficacy of oral ibuprofen and paracetamol (acetaminophen) across acute and chronic pain conditions. *Eur J Pain*. 2015 Oct;19(9):1213-1223.
PubMed: PM25530283

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Appendix — Further Information

Previous CADTH Reports

6. Pain Management Programs for Pediatric Patients with Chronic Pain Conditions: Clinical Effectiveness, Cost Effectiveness, and Guidelines. (*CADTH Rapid Response report: summary of abstracts*). Ottawa (ON): CADTH; 2020: https://www.cadth.ca/pain-management-programs-pediatric-patients-chronic-pain-conditions-clinical-effectiveness-cost

7. Research Gaps: Chronic Pain Management: Non-Pharmacological Treatments. (*CADTH Tools*). Ottawa (ON): CADTH; 2018: https://www.cadth.ca/tools/research-gaps-chronic-pain-management-non-pharmacologic-treatments

8. Evidence on Pain Management. Ottawa (ON): CADTH; 2020. https://www.cadth.ca/evidence-bundles/pain-evidence-bundle

Randomized Controlled Trials

Alternative Comparator

9. Patel JC, Patel PB, Acharya H, Nakum K, Tripathi CB. Efficacy and safety of lornoxicam vs ibuprofen in primary dysmenorrhea: a randomized, double-blind, double dummy, active-controlled, cross over study. *Eur J Obstet Gynecol Reprod Biol*. 2015 May;188:118-123.
PubMed: PM25808572

Age Unspecified

10. Yousefi M, Kavianpour M, Hesami S, Rashidi Nooshabadi M, Khadem Haghighian H. Effect of alpha-lipoic acid at the combination with mefenamic acid in girls with primary dysmenorrhea: randomized, double-blind, placebo-controlled clinical trial. *Gynecol Endocrinol*. 2019 Sep;35(9):782-786.
PubMed: PM30957578

Review Articles

11. Barbagallo M, Sacerdote P. Ibuprofen in the treatment of children's inflammatory pain: a clinical and pharmacological overview. *Minerva Pediatr*. 2019 Feb;71(1):82-99.
PubMed: PM30574736

12. Caes L, Fisher E, Clinch J, Eccleston C. Current Evidence-Based Interdisciplinary Treatment Options for Pediatric Musculoskeletal Pain. *Curr Treatm Opt Rheumatol*. 2018;4(3):223-234.
PubMed: PM30148046

Additional References

13. Reid K, Hartling L, Ali S, Le A, Norris A, Scott SD. Development and Usability Evaluation of an Art and Narrative-Based Knowledge Translation Tool for Parents With a Child With Pediatric Chronic Pain: Multi-Method Study. *J Med Internet Res*. 2017 12 14;19(12):e412.
PubMed: PM29242180