

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Gabapentinoids for Chronic Pain in Pediatric Populations: Clinical Effectiveness

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Research Question

What is the clinical effectiveness of gabapentinoids for the treatment of chronic pain in pediatric patients?

Key Findings

Two systematic reviews and three randomized controlled trials were identified regarding the clinical effectiveness of gabapentinoids for the treatment of chronic pain in pediatric patients.

Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, 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 gabapentinoids and pediatric populations. 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 January 1, 2015 and April 24, 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	Gabapentinoids (i.e., $\alpha 2\delta$ [Alpha 2 Delta] ligands; Ca^{2+} $\alpha 2\delta$ ligands; e.g., gabapentin, pregabalin)
Comparators	Other pharmacological medications (e.g., amitriptyline, nortriptyline, duloxetine, ibuprofen, naproxen, ketorolac, 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. These are followed by randomized controlled trials and non-randomized studies.

Two systematic reviews^{1,2} and three randomized controlled trials³⁻⁵ were identified regarding the clinical effectiveness of gabapentinoids for the treatment of chronic pain in pediatric patients. No relevant health technology assessments or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Two systematic reviews^{1,2} were identified regarding the clinical effectiveness of gabapentinoids for the treatment of chronic pain in pediatric patients. The systematic review by Egunsola et al.¹ contained two randomized controlled trials that met the selection criteria of this report; one study comparing gabapentin to amitriptyline for the treatment of chronic regional pain syndrome or neuropathic pain and one study comparing pregabalin to placebo for the treatment of fibromyalgia. Neither of the trials showed significant differences in their primary outcomes.¹ Similarly, the systematic review by Cooper et al.² contained two randomized controlled trials. One trial compared gabapentin to amitriptyline in pediatric patients with complex regional pain syndrome type 1 or neuropathic pain and the second trial compared pregabalin to placebo in pediatric patients with fibromyalgia.² The authors concluded that there was no evidence to support or counter the use of the gabapentinoids to treat chronic non-cancer pain in pediatric patients.²

Additionally, three randomized controlled trials³⁻⁵ were identified regarding the clinical effectiveness of gabapentinoids for the treatment of chronic pain in pediatric patients. The trial by Arnold et al.³ compared pregabalin to placebo in the treatment of adolescent patients with fibromyalgia. At 15 weeks, the authors concluded pregabalin did not significantly improve the primary outcome of mean pain score compared to placebo.³ The trial by Brown et al.⁴ compared gabapentin to amitriptyline in the treatment of pediatric patients with complex regional pain syndrome type 1 or neuropathic pain. At 6 weeks, both amitriptyline and gabapentin significantly reduced pain intensity scores and improved sleep, however, there was no statistically significant difference between the two groups.⁴ Lastly, the trial by Bakhshandeh et al.⁵ compared pregabalin to propranolol in migraine prophylaxis in pediatric patients. After 4 and 8 weeks, both pregabalin and propranolol had numerical reductions in the monthly headache frequency.⁵ There was also a significant difference in the reduction of headache frequency between the two groups.⁵

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Egunsola O, Wylie CE, Chitty KM, Buckley NA. Systematic review of the efficacy and safety of gabapentin and pregabalin for pain in children and adolescents. *Anesth Analg.* 2019 Apr;128(4):811-819.
[PubMed: PM30451725](https://pubmed.ncbi.nlm.nih.gov/30451725/)

2. Cooper TE, Wiffen PJ, Heathcote LC, et al. Antiepileptic drugs for chronic non-cancer pain in children and adolescents. *Cochrane Database Syst Rev*. 2017 Aug 5;8:Cd012536.
[PubMed: PM28779491](#)

Randomized Controlled Trials

3. Arnold LM, Schikler KN, Bateman L, et al. Safety and efficacy of pregabalin in adolescents with fibromyalgia: a randomized, double-blind, placebo-controlled trial and a 6-month open-label extension study. *Pediatr Rheumatol Online J*. 2016 Jul 30;14(1):46.
[PubMed: PM27475753](#)
4. Brown S, Johnston B, Amaria K, et al. A randomized controlled trial of amitriptyline versus gabapentin for complex regional pain syndrome type I and neuropathic pain in children. *Scand J Pain*. 2016 Oct;13:156-163.
[PubMed: PM28850523](#)
5. Bakhshandeh Bali M, Rahbarimanesh AA, Sadeghi M, Sedighi M, Karimzadeh P, Ghofrani M. Comparison of propranolol and pregabalin for prophylaxis of childhood migraine: a randomised controlled trial. *Acta Med Iran*. 2015;53(5):276-280.
[PubMed: PM26024701](#)

Non-Randomized Studies

No literature identified.

Appendix — Further Information

Non-Randomized Studies

No Comparator

6. Kaul I, Amin A, Rosenberg M, Rosenberg L, Meyer WJ, 3rd. Use of gabapentin and pregabalin for pruritus and neuropathic pain associated with major burn injury: a retrospective chart review. *Burns*. 2018 Mar;44(2):414-422.
[PubMed: PM28822592](#)
7. Hauer JM, Solodiuk JC. Gabapentin for management of recurrent pain in 22 nonverbal children with severe neurological impairment: a retrospective analysis. *J Palliat Med*. 2015 May;18(5):453-456.
[PubMed: PM25658145](#)

Mixed Intervention

8. Przekop P, Przekop A, Haviland MG. Multimodal compared to pharmacologic treatments for chronic tension-type headache in adolescents. *J Bodyw Mov Ther*. 2016 Oct;20(4):715-721.
[PubMed: PM27814849](#)

Review Articles

9. DeMoss P, Ramsey LH, Karlson CW. Phantom limb pain in pediatric oncology. *Front Neurol*. 2018;9:219.
[PubMed: PM29686645](#)
10. Gmuca S, Sherry DD. Fibromyalgia: treating pain in the juvenile patient. *Paediatr Drugs*. 2017 Aug;19(4):325-338.
[PubMed: PM28536810](#)