

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Gabapentin, Celecoxib, and Acetaminophen for the Prevention of Post-Operative Pain: Clinical Effectiveness

Service Line: Rapid Response Service
Version: 1.0
Publication Date: July 31, 2017
Report Length: 10 Pages

Authors: Calvin Young, Kelly Farrah

Cite As: Gabapentin, celecoxib, and acetaminophen for the prevention of post-operative pain: clinical effectiveness. Ottawa: CADTH; 2017 Jul. (CADTH rapid response report: summary of abstracts).

Acknowledgments:

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 are those of CADTH and do not necessarily represent the views of Canada's federal, provincial, or territorial governments 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.

Research Questions

1. What is the clinical effectiveness of pre-operative administration of gabapentin to reduce post-operative pain following orthopedic surgery?
2. What is the clinical effectiveness of pre-operative administration of celecoxib to reduce post-operative pain following orthopedic surgery?
3. What is the clinical effectiveness of pre-operative administration of acetaminophen to reduce post-operative pain following orthopedic surgery?

Key Findings

Five randomized controlled trials were identified regarding the clinical effectiveness of pre-operative administration of gabapentin, celecoxib, or acetaminophen for patients undergoing orthopedic surgical procedures.

Methods

A limited literature search was conducted on key resources including PubMed, 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. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2012 and July 25, 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	Patients undergoing orthopedic surgical procedures
Interventions	Gabapentin; Celecoxib; Acetaminophen; Alone or in any combination with each other
Comparators	Gabapentin; Celecoxib; Acetaminophen; Alone or in any combination with each other
Outcomes	Clinical effectiveness (e.g. reduced post-operative pain, reduced opioid intake post-op, improved pain control, safety)
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials

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.

Five randomized controlled trials were identified regarding the clinical effectiveness of pre-operative administration of gabapentin, celecoxib, or acetaminophen for patients undergoing orthopedic surgical procedures. No relevant health technology assessments, systematic reviews, or meta-analyses were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Five randomized controlled trials¹⁻⁵ were identified regarding the clinical effectiveness of pre-operative administration of gabapentin, celecoxib, or acetaminophen for patients undergoing orthopedic surgical procedures. One randomized controlled trial¹ compared the effectiveness of intravenous (IV) versus oral acetaminophen as part of a multimodal perioperative pain regimen.¹ Patients (n=120) were randomized to receive either IV or oral acetaminophen prior to total joint arthroplasty.¹ The authors concluded that IV delivery of acetaminophen does not provide much benefit in reducing pain or narcotic use compared to oral delivery.¹

A second randomized controlled trial² evaluated the comparative effectiveness of gabapentin versus gabapentin plus celecoxib on pain and the complication rate after laminectomy. Patients (n=114) were randomized to receive either gabapentin, gabapentin plus celecoxib, or placebo.² The authors concluded that celecoxib and gabapentin is an effective combination for pain control, with lesser side effects than gabapentin alone.²

A third randomized controlled trial³ assessed the effectiveness of two different dosages of gabapentin as part of a multimodal analgesic regime for total knee arthroscopy. Patients (n=300) were randomized to receive either 1300 mg/d gabapentin, 900 mg/d gabapentin, or placebo daily from 2 hours preoperatively to postoperative day 6.³ The authors concluded that gabapentin may have a limited (if any) role in this patient population due to little difference in pain and morphine use between the treatment groups and placebo.³

A fourth randomized controlled trial⁴ aimed to determine if adding gabapentin to celecoxib improves in-hospital rehabilitation and physical function for patients undergoing total knee arthroplasty. Patients (n=212) were randomized to receive celecoxib and either gabapentin or placebo prior to their surgery.⁴ The gabapentin group had decreased postoperative analgesic requirements and improved knee range of motion, but did not show improvement in pain or physical function.⁴

A fifth randomized controlled trial⁵ evaluated which method of administration (IV versus oral) for paracetamol is the most effective in patients undergoing knee arthroscopy. Patients (n=30) were randomized to receive either 1.0 g oral paracetamol preoperatively or 1.0 g IV paracetamol intraoperatively.⁵ The outcomes of interest were plasma paracetamol levels, postoperative pain, need for additional analgesia, and duration of stay in the recovery room.⁵ The authors concluded that IV administration of paracetamol was more reliable for achieving effective plasma paracetamol levels.⁵

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

No literature identified.

Randomized Controlled Trials

1. Politi JR, Davis RL, Matrka AK. Randomized prospective trial comparing the use of intravenous versus oral acetaminophen in total joint arthroplasty. *J Arthroplasty*. 2017 Apr;32(4):1125-7.
[PubMed: PM27839957](#)
2. Vasigh A, Jaafarpour M, Khajavikhan J, Khani A. The effect of gabapentin plus celecoxib on pain and associated complications after laminectomy. *J Clin Diagn Res [Internet]*. 2016 Mar [cited 2017 Jul 28];10(3):UC04-UC08. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4843358>
[PubMed: PM27134973](#)
3. Lunn TH, Husted H, Laursen MB, Hansen LT, Kehlet H. Analgesic and sedative effects of perioperative gabapentin in total knee arthroplasty: a randomized, double-blind, placebo-controlled dose-finding study. *Pain*. 2015 Dec;156(12):2438-48.
[PubMed: PM26230741](#)
4. Clarke HA, Katz J, McCartney CJ, Stratford P, Kennedy D, Page MG, et al. Perioperative gabapentin reduces 24 h opioid consumption and improves in-hospital rehabilitation but not post-discharge outcomes after total knee arthroplasty with peripheral nerve block. *Br J Anaesth*. 2014 Nov;113(5):855-64.
[PubMed: PM24980426](#)
5. Brett CN, Barnett SG, Pearson J. Postoperative plasma paracetamol levels following oral or intravenous paracetamol administration: a double-blind randomised controlled trial. *Anaesth Intensive Care*. 2012 Jan;40(1):166-71.
[PubMed: PM22313079](#)

Appendix — Further Information

Previous CADTH Reports

6. Medications for the management of post-surgical pain in pediatrics: guidelines [Internet]. 2016 Jul [cited 2017 Jul 28]. (CADTH rapid response report: summary of abstracts). Available from: <https://www.cadth.ca/medications-management-post-surgical-pain-pediatrics-guidelines>
7. Celecoxib for post-operative pain management: a review of the clinical benefit and harm [Internet]. 2009 Aug [cited 2017 Jul 28]. (CADTH rapid response report). Available from: <https://www.cadth.ca/celecoxib-post-operative-pain-management-review-clinical-benefit-and-harm-0>
8. Post-operative pain management for patients after elective knee or hip replacement surgery: guidelines [Internet]. (CADTH rapid response report). 2009 Nov [cited 2017 Jul 28]. Available from: https://www.cadth.ca/sites/default/files/pdf/K0102_Pain_Management_final.pdf

Systematic Reviews and Meta-Analyses

Alternate Comparator

9. Secrist ES, Freedman KB, Ciccotti MG, Mazur DW, Hammoud S. Pain management after outpatient anterior cruciate ligament reconstruction: a systematic review of randomized controlled trials. *Am J Sports Med.* 2016 Sep;44(9):2435-47. [PubMed: PM26684664](#)
10. Chaparro LE, Smith SA, Moore RA, Wiffen PJ, Gilron I. Pharmacotherapy for the prevention of chronic pain after surgery in adults. *Cochrane Database Syst Rev.* 2013 Jul 24;(7):CD008307. [PubMed: PM23881791](#)

No Comparator Specified

11. Arumugam S, Lau CS, Chamberlain RS. Use of preoperative gabapentin significantly reduces postoperative opioid consumption: a meta-analysis. *J Pain Res [Internet].* 2016 [cited 2017 Jul 28];9:631-40. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5026214> [PubMed: PM27672340](#)
12. Wang J, Liu GT, Mayo HG, Joshi GP. Pain management for elective foot and ankle surgery: a systematic review of randomized controlled trials. *J Foot Ankle Surg.* 2015 Jul;54(4):625-35. [PubMed: PM24954920](#)
13. Jones S, Merrill A. Effectiveness of intravenous acetaminophen for pain management in orthopedic surgery patients: a systematic review. *JB Libr Syst Rev.* 2012; 10(37):2490-2513. [PubMed: PM27820591](#)

Randomized Controlled Trials

Alternate Comparator

14. Bhosale UA, Yegnanarayan R, Gupta A, Shah P, Sardesai S. Comparative pre-emptive analgesic efficacy study of novel antiepileptic agents gabapentin, lamotrigine and topiramate in patients undergoing major surgeries at a tertiary care hospital: a randomized double blind clinical trial. *J Basic Clin Physiol Pharmacol*. 2017 Jan 1;28(1):59-66.
[PubMed: PM27487492](#)
15. Qadeer M, Waqas M, Rashid MJ, Enam SA, Sharif S, Murtaza G. Preventive gabapentin versus pregabalin to decrease postoperative pain after lumbar microdiscectomy: a randomized controlled trial. *Asian Spine J* [Internet]. 2017 Feb [cited 2017 Jul 28];11(1):93-8. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5326739>
[PubMed: PM28243376](#)
16. Tang J, Fan J, Yao Y, Cai W, Yin G, Zhou W. Application of a buprenorphine transdermal patch for the perioperative analgesia in patients who underwent simple lumbar discectomy. *Medicine (Baltimore)* [Internet]. 2017 May [cited 2017 Jul 28];96(20):e6844. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5440136>
[PubMed: PM28514299](#)
17. Bilir S, Yurtlu BS, Hanci V, Okyay RD, Erdogan KG, Ayoglu HP, et al. Effects of peroperative intravenous paracetamol and lornoxicam for lumbar disc surgery on postoperative pain and opioid consumption: a randomized, prospective, placebo-controlled study. *Agri*. 2016 Apr;28(2):98-105.
[PubMed: PM27225739](#)
18. Gupta A, Abubaker H, Demas E, Ahrendtsen L. A randomized trial comparing the safety and efficacy of intravenous ibuprofen versus ibuprofen and acetaminophen in knee or hip arthroplasty. *Pain Physician*. 2016 Jul;19(6):349-56.
[PubMed: PM27454264](#)
19. Khalili G, Salimianfard M, Zarehzadeh A. Comparison between paracetamol, piroxicam, their combination, and placebo in postoperative pain management of upper limb orthopedic surgery (a randomized double blind clinical trial). *Adv Biomed Res* [Internet]. 2016 [cited 2017 Jul 28];5:114. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4926544>
[PubMed: PM27403409](#)
20. Khetarpal R, Kataria AP, Bajaj S, Kaur H, Singh S. Gabapentin vs pregabalin as a premedication in lower limb orthopaedics surgery under combined spinal epidural technique. *Anesth Essays Res* [Internet]. 2016 May [cited 2017 Jul 28];10(2):262-7. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4864698>
[PubMed: PM27212758](#)

21. Zhang S, Paul J, Nantha-Aree M, Buckley N, Shahzad U, Cheng J, et al. Reanalysis of morphine consumption from two randomized controlled trials of gabapentin using longitudinal statistical methods. *J Pain Res* [Internet]. 2015 [cited 2017 Jul 28];8:79-85. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4332293>
[PubMed: PM25709496](#)
22. Khurana G, Jindal P, Sharma JP, Bansal KK. Postoperative pain and long-term functional outcome after administration of gabapentin and pregabalin in patients undergoing spinal surgery. *Spine (Phila Pa 1976)*. 2014 Mar 15;39(6):E363-E368.
[PubMed: PM24384657](#)
23. Paul JE, Nantha-Aree M, Buckley N, Cheng J, Thabane L, Tidy A, et al. Gabapentin does not improve multimodal analgesia outcomes for total knee arthroplasty: a randomized controlled trial. *Can J Anaesth*. 2013 May;60(5):423-31.
[PubMed: PM23479393](#)

Alternate Population

24. Bafna U, Rajarajeshwaran K, Khandelwal M, Verma AP. A comparison of effect of preemptive use of oral gabapentin and pregabalin for acute post-operative pain after surgery under spinal anesthesia. *J Anaesthesiol Clin Pharmacol* [Internet]. 2014 Jul [cited 2017 Jul 28];30(3):373-7. Available from:
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4152678>
[PubMed: PM25190946](#)

Mixed Intervention

25. Kim SI, Ha KY, Oh IS. Preemptive multimodal analgesia for postoperative pain management after lumbar fusion surgery: a randomized controlled trial. *Eur Spine J*. 2016 May;25(5):1614-9.
[PubMed: PM26324284](#)

Guidelines and Recommendations

26. Hip fracture: management (CG124). Clinical guideline [Internet]. London: National Institute for Health and Care Excellence (NICE); 2011 Jun [updated 2017 May; [cited 2017 Jul 28] Available from: <https://www.nice.org.uk/guidance/cg124/resources/hip-fracture-management-pdf-35109449902789>
27. Surgical Critical Care Evidence-Based Medicine Guidelines Committee. Gabapentin for acute postoperative pain [Internet]. Orlando: Department of Surgical Education, Orlando Regional Medical Center; 2016 Sep [cited 2017 Jul 28]. Available from:
<http://www.surgicalcriticalcare.net/Guidelines/Gabapentin%202016.pdf>
28. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. 2016 Feb;17(2):131-57.
[PubMed: PM26827847](#)
29. Australian and New Zealand Guideline for hip fracture care: improving outcomes in hip fracture management of adults [Internet]. Sydney: Australian and New Zealand Hip Fracture Registry Steering Group; 2014 Sep [cited 2017 Jul 28]. Available from:
<http://anzhfr.org/wp-content/uploads/2016/07/ANZ-Guideline-for-Hip-Fracture-Care.pdf>

30. Management of hip fractures in the elderly: evidence-based clinical practice guideline [Internet]. Rosemont (IL): American Academy of Orthopaedic Surgeons; 2014 [cited 2017 Jul 28]. Available from: https://www.aaos.org/research/guidelines/HipFxGuideline_rev.pdf
31. Practice guidelines for acute pain management in the perioperative setting: an updated report by the American Society of Anesthesiologists Task Force on Acute Pain Management. Anesthesiology [Internet]. 2012 Feb [cited 2017 Jul 28];116(2):248-73. Available from: <http://www.asahq.org/~media/Sites/ASAHQ/Files/Public/Resources/standards-guidelines/practice-guidelines-for-acute-pain-management-in-the-perioperative-setting.pdf>
PubMed: [PM22227789](https://pubmed.ncbi.nlm.nih.gov/22227789/)

Clinical Practice Guidelines – Uncertain Methodology

32. Clinical guideline for peri and post-operative pain control for complex pain patients [Internet]. Cornwall (United Kingdom): Royal Cornwall Hospitals NHS Trust; 2016 [cited 2017 Jul 28]. Available from: <https://doclibrary-richt.cornwall.nhs.uk/DocumentsLibrary/RoyalCornwallHospitalsTrust/Clinical/Anaesthetics/GuidelineForPeriAndPostOperativePainControlForComplexPatients.pdf>
33. Misiólek H, Cettler M, Woron J, Wordliczek J, Dobrogowski J, Mayzner-Zawadzka E. The 2014 guidelines for post-operative pain management. Anaesthesiol Intensive Ther [Internet]. 2014 Sep-Oct [cited 2017 Jul 28];46(4):221-44. Available from: <http://mnoar.med.ru/InfLet/Rek4.pdf>
PubMed: [PM25293474](https://pubmed.ncbi.nlm.nih.gov/25293474/)
34. Lowenberg D, Vokach-Brodsky L, Tanaka P, Ottestad E, Horn J-L, Derby R. Anesthesia and pain service guidelines for total hip fracture [Internet]. Stanford (CA): Stanford Medicine; 2013 [cited 2017 Jul 28]. Available from: <http://ether.stanford.edu/policies/Peri-op%20Pain%20Guidelines%20Ortho%20Hip%20fracture.pdf>
35. Korean Knee Society. Guidelines for the management of postoperative pain after total knee arthroplasty. Knee Surg Relat Res [Internet]. 2012 Dec [cited 2017 Jul 28]; 24(4): 201–207. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3526756/>
PubMed: [PM23269957](https://pubmed.ncbi.nlm.nih.gov/23269957/)

Review Articles

36. Golladay GJ, Balch KR, Dalury DF, Satpathy J, Jiranek WA. Oral multimodal analgesia for total joint arthroplasty. J Arthroplasty. 2017 May 11. [Epub ahead of print]
PubMed: [PM28705543](https://pubmed.ncbi.nlm.nih.gov/28705543/)
37. DeOrio JK, Gadsden J. Total ankle arthroplasty and perioperative pain. J Surg Orthop Adv. 2014;23(4):193-7.
PubMed: [PM25785469](https://pubmed.ncbi.nlm.nih.gov/25785469/)

38. Mathiesen O, Wetterslev J, Kontinen VK, Pommergaard HC, Nikolajsen L, Rosenberg J, et al. Adverse effects of perioperative paracetamol, NSAIDs, glucocorticoids, gabapentinoids and their combinations: a topical review. *Acta Anaesthesiol Scand*. 2014 Nov;58(10):1182-98.
[PubMed: PM25116762](#)
39. Rivkin A, Rivkin MA. Perioperative nonopioid agents for pain control in spinal surgery. *Am J Health Syst Pharm*. 2014 Nov 1;71(21):1845-57.
[PubMed: PM25320134](#)
40. Parvizi J, Bloomfield MR. Multimodal pain management in orthopedics: implications for joint arthroplasty surgery. *Orthopedics [Internet]*. 2013 Feb [cited 2017 Jul 28];36(2 Suppl):7-14. Available from: <http://www.healio.com/doiresolver?doi=10.3928/01477447-20130122-51>
[PubMed: PM23379570](#)