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Oral Ketorolac for Renal Colic in Outpatient Settings

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Rapid Review

Key Messages

What Is the Issue?

- Renal colic is a common problem that is primarily caused by kidney stones. Renal colic, specifically kidney stones, can be a recurrent condition that can negatively impact a person's quality of life and health system utilization.
- Ketorolac through IV or intramuscular routes is a common nonsteroidal anti-inflammatory drug (NSAID) used in hospital to treat renal colic. Oral ketorolac for the management of renal colic may reduce patients' need for opioids after discharge but it is unclear if it is clinically effective when compared to alternative analgesics or whether it is recommended for use in the management of people with renal colic.

What Did We Do?

- To inform decisions about oral ketorolac for the management of outpatients with renal colic, we sought to identify and summarize literature comparing the clinical effectiveness of oral ketorolac and alternative analgesics. We also searched for evidence-based guidelines that provide recommendations about the use of oral ketorolac for the management of people with renal colic.
- A research information specialist conducted literature searches of peer-reviewed and grey literature sources published between January 1, 2013, and December 4, 2023. The search was limited to English-language documents. One reviewer screened articles for inclusion based on predefined criteria.

What Did We Find?

- The tailored search for this rapid review did not find any studies evaluating the clinical effectiveness of oral ketorolac versus alternative analgesics for the management of people with renal colic in outpatient settings that met our criteria for this review. There is therefore no specific evidence available on the efficacy oral ketorolac in the management of renal colic in the community setting in this review.
- We did not find any eligible evidence-based guidelines concerning the use of oral ketorolac for the management of people with renal colic in outpatient settings. NSAIDs have been generally mentioned as an option for renal colic in the available guidance.
- Research regarding ketorolac for renal colic published since 2013 has focused on IV or intramuscular administration. Research regarding oral ketorolac focused on indications other than renal colic (e.g.,



Key Messages

postoperative pain) may be of interest; these are listed in the appendix. These studies suggest the effectiveness of ketorolac for pain management for other indications, such as pain management following endoscopy.

What Does It Mean?

- Without comparative evidence, decision-makers may want to consider how oral ketorolac is used for related indications (e.g., procedures for removing kidney stones, ureteroscopies) to examine how it performed compared with alternative analgesics.
- Research focused on the management of renal colic is needed to evaluate the clinical effectiveness of oral ketorolac and inform guidance concerning oral ketorolac in outpatient settings.

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Research Questions

1. What is the clinical effectiveness of oral ketorolac for the management of people with renal colic in outpatient settings?
2. What are the evidence-based guidelines regarding the use of oral ketorolac for the management of people with renal colic in outpatient settings?

Context and Policy Issues

What Is Renal Colic?

Renal colic is described as a severe form of flank pain that is often caused by an acute obstruction from a stone in the urinary system.¹ Renal colic is mainly caused by nephrolithiasis (kidney stones).¹ In North America and Europe, kidney stones affect 5% to 15% of the population at some point (i.e., lifetime prevalence) with a yearly incidence of 0.5%.¹ Kidney stones are more common for some individuals; for example, the prevalence of kidney stones among males is nearly double that of females.² Kidney stones can be a recurrent condition that has a significant impact on health system utilization as well as the individual's quality of life.²⁻⁴ Aside from kidney stones, renal colic may also be caused by other issues such as ureteral spasms after stent removal or after ureteroscopy.¹

What Is the Current Practice?

To ascertain the cause of renal colic, diagnosis is usually determined through a patient's history, physical exam, laboratory testing (e.g., blood and urine test), and imaging studies (e.g., ultrasound, X-ray, CT).¹ Given the acuity of this condition, the immediate intervention is analgesia (for pain) and antiemetics (for when nausea and vomiting is experienced with the pain).¹ For renal colic, NSAIDs are the first-line therapy for analgesia.¹

Among NSAIDs, ketorolac is commonly used when people present with renal colic in the emergency department.⁵⁻⁷ Ketorolac is in the NSAID class of medications used for the short-term management and treatment of moderate to severe acute onset pain that also includes pain after an operation or painful procedure.^{5,6,8} Ketorolac can be administered in multiple dose forms, including oral, intranasal, IV, and intramuscular, as well as an ophthalmic solution.^{5-7,9} If the patient is being treated in the hospital for renal colic, ketorolac would be administered via IV or intramuscular routes. For different indications, health care providers may choose to continue the patient's treatment with oral ketorolac.^{6,10}

Oral Ketorolac and Its Potential Benefits

The oral administration of ketorolac is only indicated as a continuation to IV or intramuscular therapy (e.g., prescription for oral ketorolac following discharge from the hospital).^{5,6,10} Ketorolac is intended for short-term use (< 5 days) regardless of the dosage form(s) used.^{5,6,11,12} However, ketorolac is viewed as a way to reduce the use of opioids when appropriate; opioids have unfavourable side effect profiles and have the potential for tolerance and misuse.¹² Transitioning people to oral ketorolac versus other medications as they are

discharged may reduce complications because health care providers are aware of the patient's response to other forms of ketorolac in hospital (e.g., pain control, side effects); however, it is unclear whether oral ketorolac is clinically beneficial or recommended for people with renal colic.

By conducting this review, we can explore the available evidence to determine whether oral ketorolac is a clinically effective option for the management of renal colic.

Objective

The purpose of this report is to summarize and critically appraise the evidence regarding the clinical effectiveness of oral ketorolac for the management of outpatients with renal colic. We also aimed to identify evidence-based guidelines about the use of oral ketorolac for the management of outpatients with renal colic.

Methods

Literature Search Methods

An information specialist conducted a literature search on December 4, 2023, of key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the [International HTA Database](#), the websites of Canadian and international health technology agencies, and Google. The search strategies were developed from elements of the research questions and selection criteria. They included both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. We limited the searches to English-language documents published since January 1, 2013.

The first search strategy contained concepts for ketorolac, renal colic, oral administration, and outpatients. We applied no study design search filters to the first search.

The second search strategy contained concepts for renal colic, NSAIDs, and pain management. We also applied [CADTH-developed study design search filters](#) for guidelines, health technology assessments, systematic reviews, meta-analyses, indirect treatment comparisons, and any types of clinical trials or observational studies.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, 1 reviewer screened titles and abstracts and then retrieved potentially relevant articles to assess for inclusion. [Table 1](#) presents the final selection of full-text articles based on the inclusion criteria.

Table 1: Selection Criteria

Criteria	Description
Population	People (all ages) with renal colic in outpatient settings
Intervention	Oral ketorolac (any dose)
Comparators	Q1: Alternative analgesics (e.g., alternative nonsteroidal anti-inflammatory drugs, acetaminophen, opioids) Q2: Not applicable
Outcomes	Q1: Clinical benefits (e.g., pain, need for rescue analgesia, health-related quality of life) and harms (e.g., adverse events) Q2: Recommendations regarding the appropriate use of oral ketorolac for renal colic (e.g., appropriate patient populations, treatment protocols [e.g., duration, dosage], contraindications)
Study designs	Q1: Health technology assessments, systematic reviews, randomized controlled trials, nonrandomized studies Q2: Evidence-based guidelines

Exclusion Criteria

We excluded articles if they did not meet the selection criteria outlined in [Table 1](#), were duplicate publications, or were published before 2013.

Summary of Evidence

Quantity of Research Available

[Appendix 1](#) presents the study selection details. We did not identify any eligible studies or evidence-based guidelines that met the inclusion criteria for this report. The literature mainly focused on other settings (e.g., hospital) or other routes of administration (IV, intramuscular). [Appendix 2](#) provides additional references of potential interest that did not meet the inclusion criteria.

Summary of Findings

Clinical Effectiveness of Oral Ketorolac for Renal Colic

We did not identify any relevant evidence regarding the clinical effectiveness of oral ketorolac for the management of outpatients with renal colic; therefore, no summary can be provided.

Evidence-Based Guidelines

We did not identify any evidence-based guidelines regarding the use of oral ketorolac for the management of outpatients with renal colic; therefore, no summary can be provided.

Limitations

There is a paucity of literature on the clinical effectiveness as well as evidence-based guidelines that provided recommendations on the use of oral ketorolac for the management of people with renal colic. This report is limited by the time frame used for literature searches (January 1, 2013, to December 4, 2023).

Conclusions and Implications for Decision- or Policy-Making

We did not identify any relevant literature about the clinical effectiveness of and recommendations for oral ketorolac for the management of people with renal colic in outpatient settings. We did identify research around ketorolac for renal colic focused on IV or intramuscular administration in hospital. We also found studies investigating oral ketorolac for different indications (listed in [Appendix 2](#)), including percutaneous nephrolithotomy (kidney stone removal) and ureteroscopy. For example, study authors of a double-blinded randomized controlled trial reported noninferiority of oral ketorolac versus opioids for postoperative pain control after endoscopy, with similar efficacy, safety profile, physician contact, and earlier convalescence (i.e., recuperation) between groups.¹³ While this can provide some insights into the potential clinical benefits and harms of oral ketorolac for some people, we are not able to provide conclusions on the clinical effectiveness of oral ketorolac versus alternative analgesics for the management of renal colic in outpatient settings. Likewise, we did not identify any recommendations about the use oral ketorolac for the management of outpatients with renal colic.

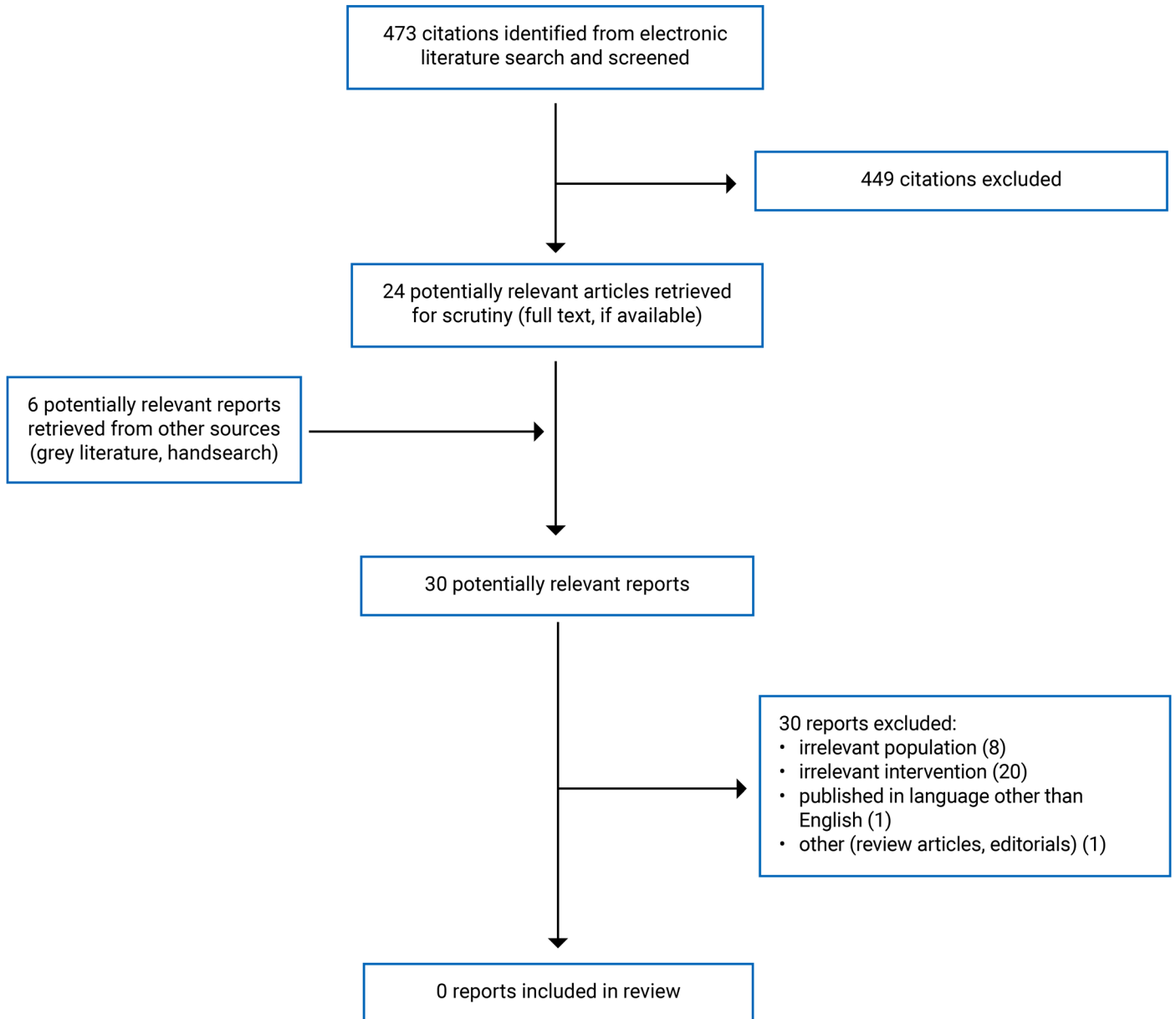
We require comprehensive research with rigorous methodological approaches for decision-making in this context. For example, we need high-quality clinical studies to inform conclusions about the potential benefits of oral ketorolac compared with alternative analgesics (e.g., alternative NSAIDs, acetaminophen, opioids), such as need for rescue analgesia and health-related quality of life. We also need evidence-based guidelines to provide recommendations on the use of oral ketorolac for the management of people with renal colic in outpatient settings.

References

1. Patti L, Leslie SW. Acute renal colic. *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023 Jan: <https://www.ncbi.nlm.nih.gov/books/NBK431091/>. Accessed 2023 Dec 19.
2. Saigal CS, Joyce G, Timilsina AR, Urologic Diseases in America Project. Direct and indirect costs of nephrolithiasis in an employed population: opportunity for disease management? *Kidney Int*. 2005;68(4):1808-1814. [PubMed](#)
3. Bryant M, Angell J, Tu H, Goodman M, Pattaras J, Ogan K. Health related quality of life for stone formers. *J Urol*. 2012;188(2):436-440. [PubMed](#)
4. Innes G, McRae A, Grafstein E, et al. Variability of renal colic management and outcomes in two Canadian cities. *CJEM*. 2018;20(5):702-712. [PubMed](#)
5. Mahmoodi AN, Kim PY. Ketorolac. *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2023 Jan: <https://www.ncbi.nlm.nih.gov/books/NBK545172/>. Accessed 2023 Dec 19.
6. Toradol. *Prescribers' Digital Reference by ConnectiveRX*. 2023; <https://www.pdr.net/drug-summary/?drugLabelId=1793>. Accessed 2023 Dec 21.
7. Rule AD, Lieske JC, Pais VM. Management of kidney stones in 2020. *JAMA*. 2020;323(19):1961-1962. [PubMed](#)
8. Ketorolac (oral route, injection route). *Mayo Clinic*. 2023 Dec 1; <https://www.mayoclinic.org/drugs-supplements/ketorolac-oral-route-injection-route/side-effects/drg-20066882?p=1>. Accessed 2023 Dec 21.
9. Chou R, Wagner J, Ahmed AY, et al. Treatments for acute pain: a systematic review. (*Comparative effectiveness review no. 240*). Rockville (MD): Agency for Healthcare Research and Quality; 2020: <https://www.ncbi.nlm.nih.gov/books/NBK566506/>. Accessed 2023 Dec 21.
10. MedlinePlus. Ketorolac. 2021; <https://medlineplus.gov/druginfo/meds/a693001.html>. Accessed 2023 Dec 21.
11. Strom BL, Berlin JA, Kinman JL, et al. Parenteral ketorolac and risk of gastrointestinal and operative site bleeding. A postmarketing surveillance study. *JAMA*. 1996;275(5):376-382. [PubMed](#)
12. Vadivelu N, Gowda AM, Urman RD, et al. Ketorolac tromethamine: routes and clinical implications. *Pain Pract*. 2015;15(2):175-193. [PubMed](#)
13. Fedrigo D, Faris A, Kachroo N, et al. SKOPE-study of ketorolac vs opioid for pain after endoscopy: a double-blinded randomized control trial in patients undergoing ureteroscopy. *J Urol*. 2021;206(2):373-381. [PubMed](#)

Appendix 1: Selection of Included Studies

Figure 1: Selection of Included Studies



Appendix 2: References of Potential Interest

Note that this appendix has not been copy-edited.

Previous CADTH Reports

Marchand DK, Loshak H. Nonsteroidal anti-inflammatory drugs and acute kidney injury: safety. (*CADTH rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2019 Jan. Ottawa (ON): CADTH; 2019; <https://www.cadth.ca/sites/default/files/pdf/htis/2019/RB1299%20NSAIDs%20and%20AKI%20Final.pdf>. Accessed Dec 21, 2023.

Ketorolac versus other non-steroidal anti-inflammatory drugs for the management of acute pain: comparative clinical effectiveness. (*CADTH rapid response report: summary of abstracts*). Ottawa (ON): CADTH; 2017; <https://www.cadth.ca/sites/default/files/pdf/htis/2017/RB1055%20Toradol%20vs%20NSAIDs%20Final.pdf>. Accessed Dec 21, 2023.

Ketorolac for pain management: a review of the clinical evidence. (*CADTH rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2014 Jun 30; <https://www.ncbi.nlm.nih.gov/books/NBK254117/>. Accessed Dec 21, 2023.

Different Indications

Khargi R, Yaghoubian AJ, Blake RM, et al. Opioid-free percutaneous nephrolithotomy: an initial experience. *World J Urol.* 2023;41(11):3113-9. [PubMed](#)

Mengers SR, Strony JT, Sivasundaram L, et al. Oral ketorolac as an adjuvant agent for postoperative pain control after arthroscopic anterior cruciate ligament reconstruction: a prospective, randomized controlled study. *J Am Acad Orthop Surg.* 2022;30(24):e1580-e1590. [PubMed](#)

Fedrigon D, Faris A, Kachroo N, et al. SKOPE-study of ketorolac vs opioid for pain after endoscopy: a double-blinded randomized control trial in patients undergoing ureteroscopy. *J Urol.* 2021;206(2):373-81. [PubMed](#)

Derwich M, Mitus-Kenig M, Pawlowska E. Orally administered NSAIDs: general characteristics and usage in the treatment of temporomandibular joint osteoarthritis: a narrative review. *Pharmaceuticals (Basel).* 2021;14(3):219. [PubMed](#)

Sivasundaram L, Mengers S, Trivedi NN, et al. Oral ketorolac as an adjuvant agent for postoperative pain control after arthroscopic rotator cuff repair: a prospective, randomized, controlled study. *J Am Acad Orthop Surg.* 2021;29(24):e1407-e1416. [PubMed](#)

DeAndrade JF, Maslanka M, Maneatis T, Bynum L, Burchmore M. The use of ketorolac in the management of postoperative pain. *Orthopedics.* 2013;17(2):157-166. [PubMed](#)

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