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European Association of Urology

Review – Stone Disease

A Systematic Review and Meta-analysis Comparing the Efficacy of Nonsteroidal Anti-inflammatory Drugs, Opioids, and Paracetamol in the Treatment of Acute Renal Colic

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Article info

Article history:
Accepted November 3, 2017

Associate Editor:
J.-N. Cornu

Keywords:
Renal colic
Urolithiasis
Analgesia
Nonsteroidal anti-inflammatory drugs
Opioids
Paracetamol
Urology
Emergency department

Abstract

Context: Renal colic is a common, acute presentation of urolithiasis that requires immediate pain relief. European Association of Urology guidelines recommend nonsteroidal anti-inflammatory drugs (NSAIDs) as the preferred analgesia. However, the fear of NSAID adverse effects and the uncertainty about superior analgesic effect have maintained the practice of advocating intravenous opioids as the initial analgesia.
Objective: The objective of this systematic review and meta-analysis was to compare the safety and efficacy of NSAIDs with opioids and paracetamol (acetaminophen) for the management of acute renal colic.
Evidence acquisition: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, World Health Organization International Clinical Trials Registry Platform, Google Scholar, and the reference list of retrieved articles were searched up to December 2016 without language restrictions. Two reviewers independently assessed eligible studies using the Cochrane Collaboration tool for assessing and reporting the risk of bias and abstracted data using predefined data fields.
Evidence synthesis: From 468 potentially relevant studies, 36 randomized controlled trials (RCTs) including 4887 patients, published between 1982 and 2016, were included in this systematic review. The treatment effect observed indicated marginal benefit of NSAIDs over opioids in initial pain reduction at 30 min (11 RCTs, $n = 1985$, mean difference [MD] −5.58, 95% confidence interval [CI] −10.22 to −0.95; heterogeneity $I^2 = 81\%$). In the subgroup analyses by the route of administration, NSAIDs required fewer rescue treatments (seven RCTs, $n = 541$, number needed to treat [NNT] 11, 95% CI 6–75) and had lower vomiting rates compared with opioids (five RCTs, $n = 531$, NNT 5, 95% CI 4–8). Comparisons of NSAIDs with paracetamol showed no difference for both drugs at 30 min (four RCTs, $n = 1325$, MD −5.67, 95% CI −17.52 to 6.18, $p = 0.35$; $I^2 = 89\%$). Patients treated with NSAIDs required fewer rescue treatments (two trials, $n = 1145$, risk ratio 0.56, 95% CI 0.42–0.74, $p < 0.001$; $I^2 = 0\%$).
Conclusions: NSAIDs were equivalent to opioids or paracetamol in the relief of acute renal colic pain at 30 min. There was less vomiting and fewer requirements for rescue analgesia with NSAIDs compared with opioids. Patients treated with NSAIDs required less rescue analgesia compared with paracetamol. Despite observed heterogeneity among the included studies and the overall quality of evidence, the findings of a lower need for rescue analgesia and fewer adverse events, in conjunction with the practical advantages of ease of delivery, suggest that NSAIDs should be the preferred analgesic option for patients presenting to the emergency department with renal colic.
Patient summary: In kidney stone–related acute pain episodes in patients with adequate renal function, treatment with nonsteroidal anti-inflammatory drugs offers effective and most sustained pain relief, with fewer side effects, when compared with opioids or paracetamol.

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https://doi.org/10.1016/j.eururo.2017.11.001
0302-2838/

1. Introduction

Renal colic is a common abdominal complaint with millions of emergency department visits worldwide due to excruciating pain. The reported prevalence of kidney stone varies widely from 0.1% to 18.5% [1], with a recurrence of stone in about 50% of cases over 5–10 yr.

Acute pain management is the main expectation of patients in severe pain from renal colic. The most important factors deciding the choice of initial analgesia include the safety, efficacy, cost, and availability of a drug, in addition to patient and clinician preferences [2]. Nonsteroidal anti-inflammatory drugs (NSAIDs) have been recommended as the first-line analgesic [3–6] based on the mechanism of action of prostaglandin synthesis inhibition and supported by the evidence of effectiveness [7]. However, NSAID use as the first-line analgesic in clinical practice has repeatedly been challenged, and many clinicians continue to prefer opioid treatment [8,9]. The practice of using opioids as the preferred analgesic in renal colic is advocated based on the advantage of titrating the dose according to pain severity and lack of adverse events such as renal failure and gastrointestinal (GI) bleeding reported with NSAID treatment [8]. Following the last Cochrane review [7] concluding that NSAID treatment achieved higher pain reductions with a superior adverse effect profile compared with opioids, some randomized controlled trials (RCTs) with contrary evidence have been published [10–12]. In addition, alternative analgesics including paracetamol have been studied. Paracetamol (acetaminophen) has been reported to provide equal [13,14] or better [15,16] analgesia than opioids for the treatment of renal colic.

The uncertainty evident in current clinical practice requires an assessment review of the efficacy and safety of analgesics commonly used in renal colic. Therefore, we aimed to compare the efficacy and safety of NSAIDs against opioids or paracetamol for the management of acute renal colic.

2. Evidence acquisition

The protocol for this systematic review was registered on PROSPERO (CRD42016047559), and the detailed methodology was published [17] following the Preferred Reporting Items for Systematic Reviews and Meta-analysis recommendations for reporting of protocols (PRISMA-P).

2.1. Literature search

Previously published Cochrane Collaboration systematic reviews [7,18] served as the foundation for our search methodology. The new search strategy was developed and published online along with the protocol [17]. MEDLINE, EMBASE, Cochrane Renal Group, and Cochrane database for systematic reviews and controlled trials were searched up to December 18, 2016, without language restrictions, to identify relevant literature. To search for unpublished or ongoing studies, the World Health Organization International Clinical Trials Registry Platform was searched through February 2017. Finally, a Google Scholar search and hand search of the reference list of retrieved articles were performed to identify missing trials or reports not published in the mainstream literature.

2.2. Inclusion and exclusion criteria

We performed an electronic literature search in identified databases separately. EndNote X7 reference manager was then used to combine the results and remove duplications. Two reviewers (S.A.P. and B.M.) independently screened the titles, abstracts, and full-text articles to identify potentially eligible studies (Fig. 1). The inclusion criteria were defined prior to the search as all RCTs, published in any language, compared NSAIDs with opioids or NSAIDs with paracetamol, in any dose and by any route, used as analgesia in acute renal colic. We translated non-English, full-text articles with the use of professional translators. The summary information for the included studies and reasoning for the excluded articles are presented in the Supplementary material.

2.3. Data extraction

Two reviewers (S.A.P. and B.M.) independently reviewed manuscripts and abstracted data using predefined data fields. We extracted data on research information (settings, study design, outcome measuring scale, and funding), characteristics of participants (age, sex, eligibility criteria, and stone confirmation method), intervention details (drug type, dose, and route of administration), and outcomes reported. The outcomes studied in this review were as follows: (1) 30-min pain variance based on patient-reported pain score using a visual analog scale (VAS 0–100 mm, VAS 10 cm) or numerical rating scale (NRS-11); (2) proportion of patients with complete pain relief at 30 min; (3) proportion of patients with $\geq$50% reduction in pain at 30 min; (4) acute adverse events such as vomiting, allergic rash, dizziness, hypotension, and respiratory problems; (5) treatment-associated vomiting rates; and (6) serious adverse events such as anaphylaxis, need for dialysis, GI bleeding, or intramuscular complications at the injection site. Long-term side effects such as cardiotoxic effects or drug dependence were not studied, as they were not considered to be relevant to single-dose initial therapy.

2.4. Assessment of risk of bias

After a calibrating exercise using the Cochrane Collaboration tool for assessing and reporting the risk of bias, two reviewers assessed each study independently. Reporting was solely based on the information published in the article and when the information reported was insufficient to make any clear judgment, the risk was reported as "unclear." Any discrepancies during the process of screening, identifying eligible articles, or risk assessments were discussed and resolved by reaching a consensus between