



# Nonsteroidal Anti-inflammatory Drugs for Managing Postoperative Endodontic Pain in Patients Who Present with Preoperative Pain: A Systematic Review and Meta-analysis

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## Abstract

**Introduction:** Nonsteroidal anti-inflammatory drugs (NSAIDs) have been commonly used to treat endodontic postoperative pain. The purpose of this study was to address the following Population, Intervention, Comparator, Outcome, Timing, Study design and setting question: in patients with preoperative pain who undergo initial orthograde endodontic treatment, what is the comparative efficacy of NSAIDs compared with non-narcotic analgesics or placebo in reducing postoperative pain and the incidence of adverse events. **Methods:** Ovid MEDLINE (1946–December 15, 2015), the Cochrane Database of Systematic Reviews (2005–December 15, 2015), and the Cochrane Central Register of Controlled Trials (to December 15, 2015) were searched using included drugs, indications, and study designs as search terms. Hand searches in texts were also conducted. Two independent reviewers assessed eligibility for inclusion, extracted data, and assessed quality using the risk of bias tool. L'Abbe plots were used for qualitative review. Where applicable, meta-analysis was conducted on the pooled effect size (ES). **Results:** Two thousand two hundred eighty-four studies were identified through the database searches; 405 full-text articles were assessed. Fifteen articles met the inclusion criteria; qualitative analysis revealed all studies had a moderate to high risk of bias. Ibuprofen was the most studied NSAID. The L'Abbe plots showed that NSAIDs are effective at relieving postoperative endodontic pain overall. Meta-analysis showed that ibuprofen 600 mg is more effective than placebo at 6 hours postoperatively (ES = 10.50,  $P = .037$ ), and ibuprofen 600 mg + acetaminophen 1000 mg combination is more effective than placebo (ES = 34.89,  $P = .000$ ) but not significantly different than ibuprofen (ES = 13.94,  $P = .317$ ). Five studies reported patients

experiencing adverse events such as drowsiness, dizziness, nausea, and emesis; 2 studies reported that patients experienced no adverse events. **Conclusions:** A combination of ibuprofen 600 mg and acetaminophen 1000 mg is more effective than placebo but not significantly different than ibuprofen 600 mg at 6 hours postoperatively. Ibuprofen 600 mg is more effective than placebo at 6 hours postoperatively; however, there are insufficient data to recommend the most effective NSAID, dose amount, or dose interval for the relief of postoperative endodontic pain of longer duration in patients with preoperative pain. (*J Endod* 2017;43:7–15)

## Key Words

Acetaminophen, endodontics, ibuprofen, meta-analysis, nonsteroidal anti-inflammatory drugs, pain, systematic review

The primary reason people seek endodontic treatment is for the relief of pain caused by bacterial infection and subsequent inflammation (1). Although pain is diminished after treatment, there may be residual symptoms because of the effects of inflammation. Endodontic treatment includes the management of postoperative pain and symptoms that address both the patient's primary concern and potential long-term complications such as chronic pain (2, 3). A variety of drugs have been used to manage postoperative pain and often include nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and combinations of drugs (4).

Pain after endodontic treatment is largely unpreventable. NSAIDs are one of the most recommended classes of pain relievers in dentistry today (5, 6). NSAIDs function by inhibiting the cyclooxygenase enzymes and preventing the generation of new prostaglandin molecules, but they have no effect against existing molecules in circulation (7).

Systematic reviews are a way to synthesize and combine data from numerous studies evaluating a common outcome (6). Holstein and Niederman (8) published a systematic

## Significance

This systematic review provides evidence that ibuprofen and ibuprofen plus acetaminophen combinations provide greater pain relief than placebo after orthograde endodontic treatment. It also emphasizes the need for increased rigor in endodontic pain research.

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review on the use of NSAIDs for treating postoperative endodontic pain in 2002 and found the most effective analgesics were a combination of flurbiprofen and tramadol or a combined regimen of preoperative and postoperative flurbiprofen. The purpose of this systematic review was to update the review from 2002 using studies published over the past 14 years, with a focus on the comparative efficacy of NSAIDs alone or in combination with other analgesics and other non-narcotic drugs for postoperative endodontic discomfort in patients who present with pre-treatment pain. This study addresses the following Population, Intervention, Comparator, Outcome, Timing, Study question: in patients with preoperative pain who undergo initial orthograde endodontic treatment, what is the comparative efficacy of NSAIDs alone or in combination with other analgesics compared with placebo or non-narcotic analgesics in reducing postoperative pain and the incidence of adverse events.

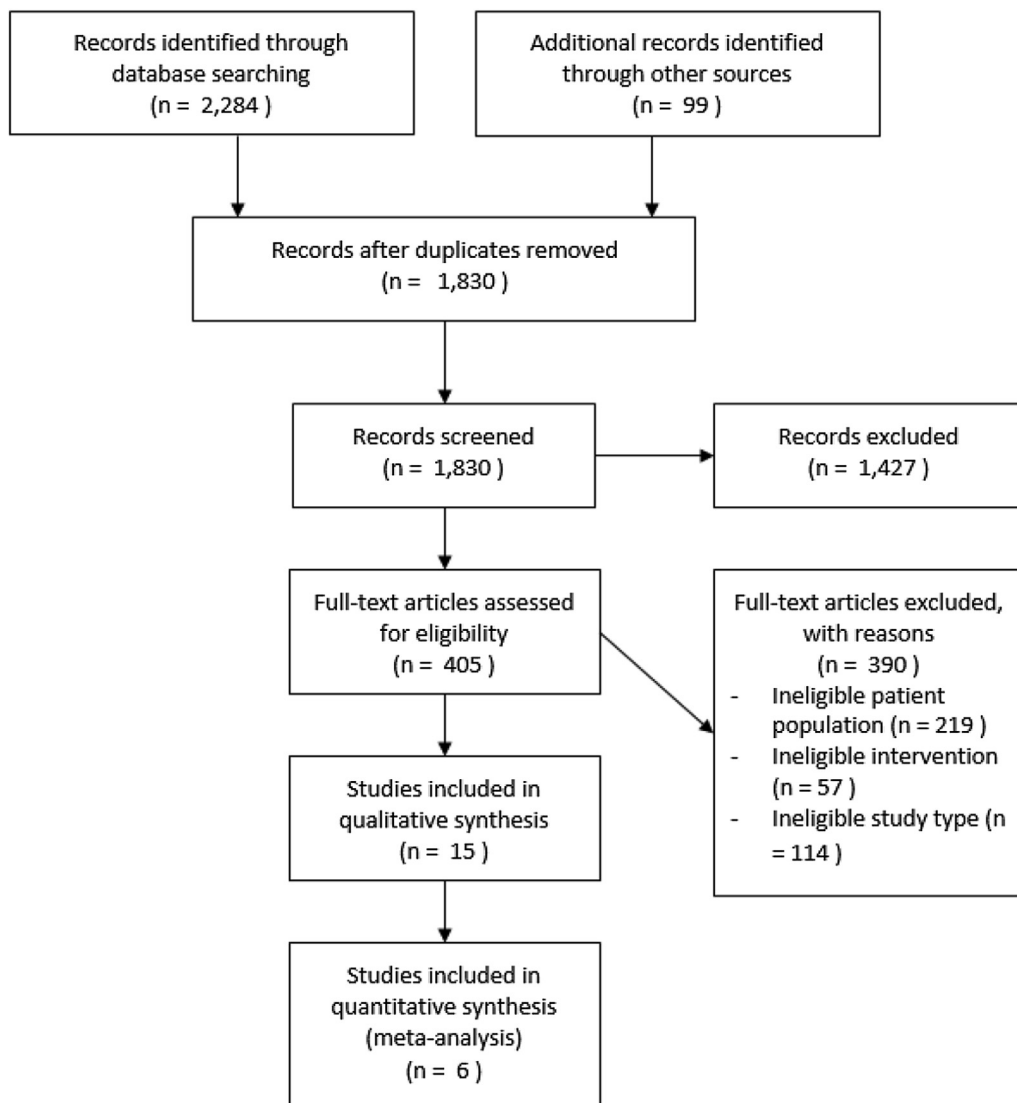
**Materials and Methods**

This systematic review was undertaken using recommended guidelines (9). A review protocol was written and registered with the public registry of systematic reviews PROSPERO (CRD42015019532).

**Literature Search**

The literature search of the Ovid MEDLINE and Ovid OLDMEDLINE, Ovid MEDLINE In-Process & Other Non-Indexed Citations, EBM Reviews—Cochrane Central Register of Controlled Trials, and EBM Reviews—Cochrane Database of Systematic Reviews included articles published from inception through December 2014. The search criteria included key words for NSAIDs and endodontic postoperative pain. Hand searching was performed on reference lists of relevant textbooks. Gray literature was also searched through [www.clinicaltrials.gov](http://www.clinicaltrials.gov). The search was repeated on December 15, 2015.

Randomized controlled trials were included if they enrolled patients who presented with endodontic pain and received a diagnosis of pulpal pathosis necessitating initial nonsurgical endodontic treatment, compared postoperative treatment with an NSAID or other non-narcotic analgesic or placebo, and measured pre- and postoperative pain. Exclusion criteria included nonrandomized studies and systematic reviews, animal studies, the use of a nonendodontic pain model, and treatment that required multiple visits.



**Figure 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

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