

Table 14. Common Medications Used for Postoperative Pain.^a

Drug	Dose, mg	NNT to achieve >50% pain relief ^b	95% CI
Acetaminophen	600/650	4.6	3.9-5.5
Acetaminophen	975/1000	3.6	3.2-4.1
Ibuprofen	400	2.5	2.4-2.6
Celecoxib	400	2.6	2.3-3.0
Naproxen	500/550	2.7	2.3-3.3
Ibuprofen + acetaminophen	200 + 500	1.6	1.5-1.8
Ibuprofen + oxycodone	400 + 5	2.3	2.0-2.8
Acetaminophen + oxycodone	1000 + 10	1.8	1.6-2.2

Abbreviation: NNT, number needed to treat.

^aAdapted from Moore et al (Summary Table B).¹⁵⁵

^bNNT for the proportion of patients with at least 50% pain relief over 4-6 hours as compared with placebo in randomized double-blind single-dose studies in patients with moderate to severe pain.

are thought to be 2 mechanisms of action. Acetaminophen has been shown to cross the blood-brain barrier and selectively inhibit the COX pathway within the brain. It has also been proposed that the analgesic properties of acetaminophen are due to modulation of the endogenous cannabinoid system. While generally a safe medication, acetaminophen overdose is now the most common cause of acute liver failure in the United States and several countries in Europe.^{133,134}

NSAIDs such as ibuprofen and naproxen are also widely used over-the-counter analgesic and antipyretic medications. The established mechanism of action for NSAIDs is to nonselectively and reversibly inhibit the cyclooxygenase isozymes COX-1 and COX-2, which are responsible for the conversion of arachidonic acid into prostaglandins and thromboxane A₂.^{135,136} Prostaglandins are important in inflammatory and pain processes; thus, inhibiting their production leads to less pain and inflammation.

Celecoxib is a selective COX-2 inhibitor most often prescribed for relief of chronic pain associated with osteoarthritis and rheumatoid arthritis.¹³⁷ It has been shown to have fewer gastrointestinal adverse effects as compared with ibuprofen or naproxen in chronically treated patients.^{138,139} In 2005 the COX-2 inhibitor rofecoxib (Vioxx) was removed from the US market after studies showed an increased risk of cardiovascular thrombotic events, including myocardial infarction and stroke.^{140,141} Celecoxib was allowed to stay on the market with warnings about the increased cardiovascular risk.¹⁴² Following conclusion of the PRECISION trial (Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen), the FDA approved a labeling supplement in 2018 for Celebrex (celecoxib), stating that it was similar to moderate doses of naproxen and ibuprofen with regard to cardiovascular safety.^{143,144} In addition to osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis, and primary dysmenorrhea, celecoxib is licensed in the United States for acute pain in adults, including postoperative pain. In a Cochrane review of 8 prospective randomized trials, 200 mg of celecoxib was found to be as effective in relieving postoperative pain as 1000 mg of acetaminophen,

and 400 mg of celecoxib was at least as effective as 400 mg of ibuprofen.¹⁴⁵

Use of nonopioid medications such as acetaminophen and/or NSAIDs has been shown to decrease or even eliminate the amount of opioid medications needed in the postoperative period.¹⁴⁶⁻¹⁵¹ Patients enrolled in opioid-sparing protocols for pain management after common otolaryngologic procedures report a high level of satisfaction with pain control, even when using minimal or no opioids.^{147,151-153} Several authors have concluded that there is limited or even zero opioid requirement for most procedures, including thyroid/parathyroid surgery, endoscopic sinus surgery, and septoplasty/rhinoplasty.¹⁵¹⁻¹⁵⁴ (**Table 4**).

Randomized prospective acute postoperative pain trials measure efficacy by comparing the number of patients needed to treat (NNT) to achieve at least 50% maximum pain relief over 4 to 6 hours. The smaller the NNT, the more efficacious the medication. **Table 14** compares several common medications used for postoperative pain (adapted from Summary Table B from Moore et al¹⁵⁵). The table demonstrates that combinations of acetaminophen and ibuprofen were more effective at relieving pain as compared with either drug alone. Despite the general belief that opioids provide better pain relief than nonopioids, combinations of either acetaminophen or ibuprofen with the opioid oxycodone were not more effective at relieving pain than the combination of acetaminophen and ibuprofen. Randomized prospective trials have shown that multimodal therapy involving simultaneous use of combinations of several medications acting at different receptors is associated with superior pain relief and decreased consumption as compared with use of a single medication.^{146,148,156} Gabapentin is sometimes recommended in addition to other pain medications. Studies similar to those summarized in **Table 14** have calculated the NNT for gabapentin 250 mg to be 11 (95% CI, 6.4-35).¹⁵⁵

The optimum timing of postoperative pain medication is unknown, particularly with regard to the question of as-needed versus fixed schedule analgesics. Although data are limited, anesthesia and pain management guidelines recommend