

Non-Opioid Acute Care Pain Management – Adults

Rationale for Nonsteroidal Anti-inflammatory Drugs (NSAIDs) & Acetaminophen in Acute Postoperative Pain Management

Postoperative pain should be managed with a multimodal approach that emphasizes non-opioid medications. NSAIDs and acetaminophen should be used together as first-line medications for postoperative pain in surgical patients, unless patients have contraindications or high risk of adverse effects.

Summary and Recommendation Overview

- NSAIDs and acetaminophen should be used together as first-line medications for postoperative pain in surgical patients
- Both NSAIDs and acetaminophen decrease postoperative pain compared to the use of opioids alone, and they decrease pain to an even greater extent when both are used simultaneously. They also reduce opioid consumption.
 - Reducing opioid consumption reduces potential for opioid related adverse drug effects such as constipation, nausea/vomiting, respiratory depression, sedation, confusion and altered mental status, and risk for potential overdose
- When using NSAIDs and acetaminophen for postoperative pain:
 - Prescribe around-the-clock dosing (scheduled dosing rather than as needed) to achieve a consistent level of pain relief
 - Concomitant use of both NSAIDs and acetaminophen by patients is appropriate because they have differing mechanisms of action
 - NSAIDs and acetaminophen are safe for most patients when given for acute pain in the postoperative period, unless contraindications exist
- Medication selection, dose, route, and duration of therapy should be individualized

NSAID Contraindications, Special Populations, and Prescriber Information

Contraindications	<ul style="list-style-type: none"> ● Avoid perioperative use for coronary artery bypass graft (CABG) surgery due to increased risk of MI and stroke [US Boxed Warning] ● Prior hypersensitivity reaction to aspirin or other NSAID
Special Populations	<ul style="list-style-type: none"> ● Elderly patients ≥ 65 years old are at increased risk for GI related adverse events - use the lowest effective dose for the shortest possible duration ● NSAIDs are NOT recommended in the following patients: <ul style="list-style-type: none"> ○ Pregnant patients ○ Active intracranial hemorrhage, active GI bleed, or in patients with thrombocytopenia or coagulation disorder ○ Patients with significant renal function impairment
Prescriber Information	<ul style="list-style-type: none"> ● Patient response may vary among NSAIDs. If your patient is having inadequate pain control consider from an appropriately dosed NSAID, consider switching to a different NSAID ● Adverse effects from NSAIDs are usually dose dependent, occur from chronic use, and there are limited data to support these same adverse effects with acute postoperative pain NSAID use. Hence, most experts believe short courses of NSAIDs for acute pain are safe.

NSAID Adverse Effect Concerns

Concern Category	Supporting Information	Recommendation
Cardiovascular Events	<ul style="list-style-type: none"> ● NSAIDs including COX-2 inhibitors may increase CV risk such as HTN, stroke, MI, and heart failure ● Naproxen, ibuprofen, and moderate dose celecoxib may have a lower risk 	Use caution in patients with history of heart failure or recent MI.
Gastrointestinal Events	<ul style="list-style-type: none"> ● GI events have not been adequately studied in the acute perioperative period ● Although NSAIDs have been shown to have GI related risks (inflammation, bleeding, ulceration, or perforation), this risk is low ● Risk increases with longer use and in patients with multiple risk factors 	Use caution in patients with history of peptic ulcer disease, history of GI bleeding, H.pylori infection, concomitant corticosteroids or anticoagulant use, patients receiving NSAIDs for a long duration or high doses before surgery, and those over 65 years of age. Consider NSAID + PPI for patients with 1+ of these risk factors.
Renal Injury	<ul style="list-style-type: none"> ● Risk factors for NSAID related acute kidney injury (AKI) include: advanced stage CKD, elderly, volume depletion, high cumulative dose exposure, concurrent calcineurin inhibitor use, and concurrent use of diuretic and/or renin angiotensin aldosterone system inhibitor 	Assess renal risk factors and avoid in advanced stage CKD. Routine labs for kidney function such as SCr and BUN are not necessary for every patient and should be ordered if renal history is unclear based on provider medical history review and discussion with the patient.
Bone Healing/ Nonunion	<ul style="list-style-type: none"> ● There are limited high quality clinical studies in humans to suggest a negative effect of NSAID exposure on bone healing or nonunion in the acute postoperative period 	Use the lowest effective dose for the shortest duration possible and weight the risks of opioid exposure to the patient.
Hematologic/ Bleeding Events	<ul style="list-style-type: none"> ● Excluding aspirin, all other NSAIDs reversibly_ inhibit platelet aggregation ● Literature suggests there is no increased risk of bleeding in the postoperative period with celecoxib or ibuprofen ● Ketorolac evidence is inconclusive 	Assess patients for coagulation disorders and anticoagulation status in the perioperative period. Many patients will benefit from a short duration of NSAID in the postoperative period.
Anastomotic Leakage	<ul style="list-style-type: none"> ● Limited literature available with conflicting results evaluating anastomotic leakage <ul style="list-style-type: none"> ○ Few adequately powered RCTs ○ Inconclusive whether rate of anastomotic leak with NSAID exposure differs from the general incidence of anastomotic leak in colorectal surgeries 	Assess patients for general risk of anastomotic leak and risk of opioid related adverse drug events in the perioperative period. Many patients will benefit from a short duration of NSAID in the postoperative period.

AKI=acute kidney injury, COX-2 = cyclooxygenase 2 inhibitor, CKD=chronic kidney disease, CV=cardiovascular, HTN = hypertension, MI = myocardial infarction, PPI = proton pump inhibitor, RCT = randomized controlled trial

Acetaminophen Contraindications, Special Populations, and Prescriber Information

Contraindications	<ul style="list-style-type: none"> • IV: prior hypersensitivity reaction to acetaminophen, severe hepatic impairment, or severe active liver disease • OTC Oral: avoid use with other medications containing acetaminophen or if allergic to the formulation
Special Populations	<ul style="list-style-type: none"> • Geriatric patients - Dose adjustments are not recommended in the perioperative period • Pregnant patients - Safe for most patients in the perioperative period however, patients should discuss the risks and benefits with their obstetrician
Prescriber Information	<ul style="list-style-type: none"> • Acetaminophen from all sources including combination products and cough/cold medications should not exceed 4000 mg/day for most adult patients

IV = intravenous, mg=milligram, OTC = over the counter

Acetaminophen Adverse Effect Concerns

Concern Category	Supporting Information	Recommendation
Hepatic & G6PD Deficiency	<ul style="list-style-type: none"> • Patients with hepatic impairment, active liver disease, G6PD deficiency, and patients with active alcohol use are at increased risk for hepatic injury due to impaired metabolism of acetaminophen at usual doses • Do not exceed 4000 mg/day of acetaminophen from all sources (prescription and OTC combination products including cough/cold medications) 	<p>Use caution in liver disease, active alcohol use, or G6PD deficiency.</p> <p>Consider dose reduction to 2000 mg/day in patients with liver disease in the perioperative period.</p>

G6PD = glucose-6-phosphate-dehydrogenase

FREQUENTLY ASKED QUESTIONS

1. Can acetaminophen and an NSAID be taken concomitantly?
 - Answer: Yes, NSAIDs and acetaminophen have differing mechanisms of action and may be taken together for pain management. It is not necessary to take these medications at alternating intervals.
2. Can I prescribe NSAIDs or acetaminophen for my postoperative patient even if these medications can be purchased over the counter?

Answer: Yes, providers prescribing NSAIDs and acetaminophen for the postoperative patient is recommended when these medications are indicated. When prescribed rather than recommended over the counter, patients may be more adherent to taking these medications postoperatively as part of their multimodal pain management regimen. Patients may discuss with the pharmacist as to costs for prescription versus over-the-counter purchases.
3. How should I counsel my patient to take acetaminophen if they are prescribed oxycodone-acetaminophen (Percocet) or hydrocodone-acetaminophen (Norco)?
 - a. Answer: Review the milligram amount of acetaminophen in each dose of acetaminophen-opioid medication with the patient. Discuss with the patient the exact milligram amount of additional acetaminophen that may be safely taken in addition to their combination acetaminophen-opioid medication so the maximum daily limit is not exceeded (acetaminophen 4000 mg/day from all sources for patients without liver dysfunction). Instruct the patient to avoid other acetaminophen containing medications. Alternatively, consider an opioid that

does not have acetaminophen, e.g. oxycodone 5mg, hydromorphone (Dilaudid) 2mg.

4. What are the common dosage formulations, strengths, and dosing for NSAIDs and acetaminophen?

Medication*	Common Dosage Forms and Strengths	Usual Adult Dosing
Ibuprofen	Tablet: 200 mg, 400 mg, 600 mg, 800 mg Chewable tablet: 100 mg Oral suspension: 100 mg/5 mL	400-800 mg three or four times daily (Max 3200 mg/day)
Naproxen	Tablet: 250 mg, 375 mg, 500 mg Oral suspension: 125 mg/5 mL	250-500 mg two or three times daily (Max 1500 mg/day)
Ketorolac	Tablet: 10 mg	10 mg four times daily (Max 40 mg/day)
Meloxicam	Tablet: 7.5 mg, 15 mg	15 mg once daily or 7.5mg twice daily (Max 15 mg/day)
Celecoxib	Capsule: 50 mg, 100 mg, 200 mg, 400 mg	100-200 mg twice daily (Max 400 mg/day)
Acetaminophen	Tablet/Capsule: 325 mg, 500 mg Controlled release tablet: 650 mg Chewable tablet: 80 mg Oral solution/suspension/liquid: 160 mg/5 mL	1000 mg four times daily (Max 4000 mg/day)

*Medication selection, dose, route, and duration of therapy should be individualized.

Selected References

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