

May 2018 ~ Resource #340520

Analgesics for Acute Pain

Acute pain results from trauma or acute illness (e.g., renal colic, heart attack, sickle cell crisis).^{4,20} As opposed to chronic pain, its etiology and location is usually clear.⁴ Acute pain is self-limited, improving over hours to weeks as the injury heals.⁴ Treatment minimizes detrimental physiologic responses (e.g., tachycardia, shallow breathing, immobility, muscle spasms, ileus, impaired immune response), adverse psychological effects (e.g., anxiety, fear), and progression to chronic pain.^{3,4,20} Set realistic goals for pain relief and function; complete pain relief may not be a realistic goal, such as after major surgery.³ Acute use of opioids turns into chronic use in 50% of patients,³⁰ so consider screening patients for drug or alcohol abuse before prescribing even short-term opioids. Research is ongoing to develop guidelines for post-op opioid prescribing to address over-prescribing and reduce potential for abuse.^{67,68} Perioperatively, different medications and routes are combined (i.e., a multimodal or balanced approach) to increase efficacy and decrease side effects.^{3,56} See our chart, *Treatment of Acute Low Back Pain*, for specifics regarding this disorder. For pain management in kids, see our chart, *Analgesics in Kids: FAQs*. The charts below review various analgesics to treat different types and severities of acute pain in adults. The first chart reviews preferred or first-line analgesics for acute pain. The second chart reviews other analgesic options that can be considered for use in patients with acute pain.

Abbreviations: CABG = coronary artery bypass graft; ED = emergency department; IV = intravenous; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug; PCA = patient-controlled analgesia; SSRI = selective serotonin reuptake inhibitor.

Preferred Analgesics for Acute Pain

Drug or Drug Class	Consider for...	Comments
NSAID (e.g., ibuprofen 400 mg every four to six hours)	<ul style="list-style-type: none"> • Mild to moderate pain from:^{3,6,16} <ul style="list-style-type: none"> • Abdominal surgery • Dental surgery • Episiotomy • Musculoskeletal injury • Orthopedic surgery • Use WITH acetaminophen for better efficacy (e.g., [adults] acetaminophen 500 to 1,000 mg WITH ibuprofen 200 to 400 mg every six hours as needed).¹⁷ 	<ul style="list-style-type: none"> • One in two to three patients with moderate to severe pain has a 50% reduction in pain over four to six hours.¹ • Ibuprofen 800 mg is NOT much more effective than ibuprofen 400 mg.^{1,7} • Reserve an injectable NSAID (e.g., diclofenac [U.S.], ibuprofen, ketorolac) for patients unable to take an oral NSAID.⁸ <ul style="list-style-type: none"> • Injectable ketorolac is equally effective compared to oral ibuprofen for moderate to severe pain.⁴⁰ • Topical NSAIDs may work as well as oral NSAIDs for acute musculoskeletal pain (e.g., sprain).¹⁶ <ul style="list-style-type: none"> • For more on topical NSAIDs and other topical pain relievers, see our chart, <i>Topicals for Pain Relief</i>. • In the U.S., NSAIDs are contraindicated for perioperative pain due to CABG.
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Drug or Drug Class	Consider for...	Comments
NSAIDs, continued	<ul style="list-style-type: none"> • Opioid-sparing effect in more severe pain.³ 	<ul style="list-style-type: none"> • Oral ketorolac has similar efficacy to other NSAIDs, but the risks associated with its use outweigh the possible benefits.⁵⁷⁻⁵⁹ • Occasional or short-term use of OTC ibuprofen or naproxen should be safe for most stable patients.^{9,15} • Avoid CHRONIC use of NSAIDs in patients with heart failure, or diabetic or other chronic kidney disease.^{5,9,10,24,39} <ul style="list-style-type: none"> • If an NSAID is needed in patients taking an ACEI, ARB, or diuretic, consider checking serum creatinine and potassium weekly for several weeks.^{11,12} • If possible, avoid NSAID use in patients with high gastrointestinal risks:¹³ <ul style="list-style-type: none"> • History of complicated ulcer, especially recent. • Patients taking anticoagulants or corticosteroids. • Patients with more than two risk factors: age over 65, high-dose NSAID, history of uncomplicated ulcer, or use of aspirin or other antiplatelet agent (e.g., clopidogrel [<i>Plavix</i>]).
Acetaminophen	<ul style="list-style-type: none"> • Patients for whom an NSAID is indicated (see above), but not desirable. • Use WITH an NSAID for better efficacy (e.g., acetaminophen 500 to 1,000 mg WITH ibuprofen 200 to 400 mg every six hours as needed in adults).¹⁷ 	<ul style="list-style-type: none"> • One in three to four patients with moderate to severe pain has a 50% reduction in pain over four to six hours with acetaminophen 1,000 mg.¹ • Acetaminophen 1,000 mg is NOT more effective than acetaminophen 500 mg.¹ • In chronic liver impairment, limit the total daily dose to 2 to 3 grams (instead of the usual 4 gram max adult daily dose).^{14,37} • Reserve parenteral acetaminophen for patients unable to take it orally or rectally. There is no evidence of superior efficacy with IV administration and it is MUCH more expensive (~\$0.10/day [oral], \$160/day [IV]).^{41,61.a}
Gabapentin	<ul style="list-style-type: none"> • The greatest benefit has been seen with preoperative doses given for abdominal, breast, and lumbar disk surgeries.^{47,54,55} 	<ul style="list-style-type: none"> • Preoperative gabapentin may reduce post-operative opioid requirements.^{46,47} • Most patients receive gabapentin 300 to 1,200 mg one to three hours prior to surgery.⁴⁷ <ul style="list-style-type: none"> ○ Some studies continued gabapentin for a few doses, post-op (e.g., 600 mg for two to four additional doses).⁴⁷ ○ Common side effects include nausea, dizziness, and sedation.⁴⁷

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Drug or Drug Class	Consider for...	Comments
<p>Strong oral opioids (e.g., hydrocodone, oxycodone)</p>	<ul style="list-style-type: none"> Moderate to severe pain (e.g., dental pain, postoperative pain, pain due to trauma, musculoskeletal pain) not relieved by nonopioids, assuming patient can take oral medications.^{3,18,20,56} 	<ul style="list-style-type: none"> Not proven more effective than ibuprofen 400 mg at achieving 50% reduction in moderate to severe pain.¹ Do not use extended-release opioids for acute pain.¹⁹ May be equally effective compared to IV opioids, even after significant surgeries (e.g., cardiac surgery).⁴³ Prescribe only enough for the anticipated duration of severe pain. Three to seven days is often enough.⁶⁵ Advise patients to wean off the opioid to over-the-counter (OTC) analgesics (e.g., acetaminophen, NSAIDs) as their pain resolves.¹⁹ Oral opioids work just as well as IV opioids, but IV opioids have a quicker onset of action, allowing for faster titrations.⁵⁶
<p>Parenteral opioids (IV, epidural, or spinal [intrathecal])</p>	<ul style="list-style-type: none"> Moderate or severe pain after invasive surgery (e.g., open abdominal surgery).³ Moderate or severe postoperative pain in patient who cannot take oral medications.^{3,56} Moderate to severe pain due to major trauma, MI (despite nitroglycerin), burns, or biliary colic.^{20,35} 	<ul style="list-style-type: none"> Consider combining with nonopioids to provide better analgesia and minimize side effects (e.g., opioid-sparing effect).³ Follow policies to get pain service approval before adding a systemic opioid to a regional (e.g., epidural, spinal) opioid. PCAs may be preferred over intermittent dosing or continuous infusion due to improved pain control (despite lower doses), improved tolerability, and patient satisfaction (e.g., post-op patients).³ Use our chart, <i>Equianalgesic Dosing of Opioids for Pain Management</i>, for help with initial IV dosing, converting between opioids, or converting from IV to oral opioids once pain is controlled and oral intake is tolerated. Ensure safe antithrombotic management in patients receiving regional anesthesia. <p>Fentanyl:</p> <ul style="list-style-type: none"> Can use fentanyl for patients with true allergy to morphine or hydromorphone.⁴² Consider when only a short duration of action is needed (e.g., procedures) as a fentanyl epidural lasts about 4 hours.⁷¹ Consider in patients with severe renal impairment or chronic kidney disease requiring a parenteral opioid, as fentanyl does not significantly accumulate with renal impairment.⁵³ <p>Hydromorphone</p> <ul style="list-style-type: none"> May be an alternative to fentanyl in patients with severe renal impairment. However, doses should be adjusted for CrCl <60 mL/min.⁵³

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Drug or Drug Class	Consider for...	Comments
Parenteral opioids, continued		<p>Morphine:</p> <ul style="list-style-type: none"> • Use IV morphine with caution in acute MI patients with bradycardia, right ventricular infarct, or hypotension.^{42,69} • Try to avoid IV morphine in renal failure due to potential for drug accumulation and toxicity (e.g., sedation, respiratory depression, hypotension).⁴² <ul style="list-style-type: none"> • If morphine is used in patients with impaired renal function, start with lower doses and titrate up slowly.⁴² • Intrathecal or epidural morphine can last up to 24 hours.^{3,71}
Local Anesthetics (e.g., bupivacaine, ropivacaine, lidocaine, mepivacaine)	<ul style="list-style-type: none"> • Perioperative use in patients at high risk from opioids or general anesthesia (e.g., pulmonary disease, morbid obesity).^{3,33} • Opioid-sparing effect.²¹ • Abdominal surgery, carotid endarterectomy, upper extremity surgery, hand surgery (peripheral nerve block).^{3,36,38} • Deep laceration repair or surgical site pain (local infiltration).^{3,31} 	<ul style="list-style-type: none"> • Routes of administration include epidural, spinal (intrathecal), peripheral nerve block, or local infiltration.³ • Elastomeric pumps (e.g., <i>On-Q</i>) can provide continuous infusion of local anesthetics to the surgical site for up to five days.³¹ • For epidural administration, local anesthetics are often combined with an opioid to reduce the amount of local anesthetic needed.⁷⁰ Anesthetic alone may be used in morbidly obese to reduce risk of respiratory depression.³³ • Liposomal bupivacaine (<i>Exparel</i> [U.S.]) is indicated for single-dose infiltration at the surgical site and lasts up to 24 hours (vs six hours for regular bupivacaine).^{21,22,32} <ul style="list-style-type: none"> • Expensive; \$315 per dose vs a few dollars for regular bupivacaine.^a • Avoid repeat bupivacaine doses, or other local anesthetics, for at least 96 hours after administration of <i>Exparel</i> due to persistence of bupivacaine in the systemic circulation and potential for overdose.²² • Data do not demonstrate consistent nor substantial clinical advantages with use of liposomal bupivacaine over other local anesthetics.⁶⁶ • Ensure safe antithrombotic management in patients receiving regional anesthesia. <p>Systemic use:</p> <ul style="list-style-type: none"> • IV lidocaine may be most beneficial for patients undergoing abdominal surgeries in reducing early post-op pain and opioid use.³⁸ <ul style="list-style-type: none"> • See our chart, <i>Intravenous Lidocaine for Pain Management</i>, for information about dosing and monitoring with IV lidocaine for pain. • Use our clinical resource, <i>Safe Use of Local Anesthetics Checklist</i>, to minimize risks associated with local anesthetics.

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Drug or Drug Class	Consider for...	Comments
Ketamine	<ul style="list-style-type: none"> Severe post-op pain in ICU patients.⁶⁰ Acute, chronic, or refractory pain in patients presenting to the ED (e.g., long-bone fractures, back pain, abdominal pain).⁶² 	<ul style="list-style-type: none"> Limited data suggest that low-dose IV ketamine (<1 mg/kg) may provide similar pain relief compared to opioids in the ED for pain from a variety of causes.^{62,64} <ul style="list-style-type: none"> Ketamine may be associated with more neuropsychological side effects compared to opioids (e.g., agitation, hallucinations, dysphoria, confusion).⁶⁴ IV ketamine may provide an opioid-sparing effect, especially in surgeries associated with severe post-op pain (e.g., abdominal or thoracic surgeries).^{27,60} <ul style="list-style-type: none"> See our commentary, <i>Ketamine for ICU Analgesia and Sedation</i>, for details on ketamine efficacy, safety, and patient selection.

a. Costs are based on wholesale acquisition cost (WAC). Pricing by Elsevier, accessed April 2018.

Not Preferred for Acute Pain

Drug or Drug Class	Comments
Buprenorphine (partial agonist [mu]/antagonist [kappa])	<ul style="list-style-type: none"> Buprenorphine is a mixed opiate with partial agonist and antagonist activity.⁴² Parenteral buprenorphine 0.3 mg is considered equivalent to parenteral morphine 10 mg for acute pain.⁴⁴ Buprenorphine might be a safer choice than a full opioid in patients with respiratory depression. <ul style="list-style-type: none"> Doubling the dose from 0.3 mg to 0.6 mg may improve analgesia without increasing respiratory depression.⁴⁴ See our chart, <i>FAQs About Buprenorphine for Chronic Pain</i>, for more on buprenorphine, including why sublingual, buccal, and transdermal buprenorphine products should NOT be used for acute pain.
Codeine	<ul style="list-style-type: none"> Codeine is metabolized to morphine via CYP2D6.² <ul style="list-style-type: none"> Genetic polymorphisms may result in poor response to codeine (poor metabolizers) or toxicity (ultrarapid metabolizers).^{2,23} Efficacy of codeine is reduced by strong CYP2D6 inhibitors (e.g., bupropion, fluoxetine).²³ Avoid codeine in children and breastfeeding women.^{45,48} <ul style="list-style-type: none"> See our chart, <i>Analgesics in Kids: FAQs</i>, for more about the risks of codeine in children.
Fentanyl (non-injectable formulations [e.g., patches, transmucosal lozenge, buccal tablet, nasal spray])	<ul style="list-style-type: none"> Reserve the non-injectable fentanyl products for patients with chronic pain who are opioid-tolerant (e.g., have been taking the equivalent of at least 60 mg of morphine daily for at least one week) due to risk of toxicity, including respiratory depression.^{34,50}

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Drug or Drug Class	Comments
Meperidine	<ul style="list-style-type: none"> • Meperidine has a neurotoxic metabolite, normeperidine. Normeperidine may accumulate with repeated meperidine dosing, especially in patients with renal or hepatic impairment and in the elderly.^{28,29} • Side effects of meperidine may include seizures, myoclonus, tremor, confusion, dysphoria, and delirium.^{28,42} • Naloxone is not effective for treating normeperidine toxicity, and in fact may worsen it.²⁹ • Use meperidine with caution in patients with arrhythmias due to risk of an increased rate of ventricular response.⁴² • Use with caution in patients taking other serotonergic meds (e.g., SSRIs, cyclobenzaprine) due to risk of serotonin syndrome.³
Other mixed agonist/antagonists (e.g., butorphanol, nalbuphine)	<ul style="list-style-type: none"> • Analgesic effects of partial agonists (kappa)/antagonists (mu) are limited by a dose ceiling.⁵¹ • Avoid in opioid-tolerant patients, as use may lead to withdrawal symptoms (e.g., anxiety, agitation, dysphoria).⁴² • Butorphanol use is often reserved for pain when other options are not effective, tolerated, or inadequate.⁶³ <ul style="list-style-type: none"> • Use may also be limited by adverse effects (e.g., psychotomimetic effects) and prolonged respiratory depression at higher doses.⁶³ • Nalbuphine efficacy and safety data compared with morphine are inconsistent.⁵² <ul style="list-style-type: none"> • Avoid doses greater than 20 mg/dose, especially in opiate-naïve patients.⁴² • Nalbuphine may be associated with less itching and less respiratory depression compared to morphine.⁵² • See our chart, <i>Equianalgesic Dosing of Opioids for Pain Management</i>, for equivalent doses, other considerations, and potential side effects.
Tramadol	<ul style="list-style-type: none"> • One in eight patients with moderate to severe pain has a 50% pain reduction over four to six hours with tramadol.¹ • Efficacy of tramadol is reduced in poor CYP2D6 metabolizers and by strong CYP2D6 inhibitors.²³ • Tramadol has many drug interactions (e.g., SSRIs), including additive serotonergic side effects (e.g., nausea, central nervous system stimulation).⁴² • Tramadol can lower the seizure threshold.²⁵ • Maximum adult daily dose 300 mg or 400 mg, depending on product.^{25,26} • See product labeling for dosing in elderly patients, or in patients with renal or hepatic dysfunction. • Avoid tramadol in children and breastfeeding women.^{45,49} <ul style="list-style-type: none"> • See our chart, <i>Analgesics in Kids: FAQs</i>, for more about the risks of tramadol in children.

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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