Introduction

Opioid analgesics are advocated and widely prescribed for the management of moderate to severe postsurgical pain. However, in recent years, opioids have been increasingly advocated as analgesics for breakthrough pain in patients treated with regional anesthesia and multimodal analgesia rather than administered around the clock as primary monotherapy. In the immediate postoperative period, patients are usually treated with patient-controlled analgesia or caregiver-administered parenteral opioids, titrated to the intensity of the pain complaint. As soon as patients are able to tolerate a liquid diet, they should be advanced to orally administered opioids, which can be continued during the convalescent and rehabilitative periods following surgery. Morphine and oxycodone are primarily used in inpatient settings; however, hydromorphone, hydrocodone, and most recently tapentadol, offer therapeutic alternatives for patients experiencing inadequate pain control or intolerable adverse effects.

The advantages and disadvantages of parenteral and oral opioids are presented in Table 7.1.

Parenteral Opioids

Morphine

Parenterally administered morphine remains the standard of care for control of acute pain following surgical and traumatic injuries. Ten mg to 15 mg of parenteral morphine, in divided doses, is generally recommended as a starting dose for moderate to severe surgical pain in patients weighing >50 kg. Onset of analgesia with IV morphine is noted within 5 to 15 minutes, while duration ranges from 2 to 4 hours, depending upon dose administered. Small doses of IV morphine (2 mg to 3 mg every 1 to 2 hours) may be administered for breakthrough pain in patients treated with continuous regional blockade. Parenteral boluses of morphine may also be administered to patients who were initially treated with IV-PCA morphine or epidural analgesia, yet remain NPO.

Morphine is associated with clinically significant dose-dependent adverse effects. These include annoying side effects such as nausea, vomiting, and pruritus, and serious, occasionally life-threatening side effects such as excessive sedation and respiratory depression. Oral and IV doses of morphine release histamine, which may precipitate hypotension and bronchospasm. Morphine also increases smooth muscle tone and may induce or exacerbate biliary, tubular, and ureteral colic. Like other opioid agonists, morphine’s effect on respiratory drive will increase PaCO₂ and may raise intracranial pressure. Morphine’s principal metabolite (morphine-6-glucuronide) has significant potency and is primarily excreted in the urine. For this reason, it should not be administered to patients with acute renal failure.

Hydromorphone (Dilaudid)

Parenteral doses of hydromorphone provide rapid and powerful control of postsurgical pain. Following slow IV administration, analgesia is noted in 2 to 5 minutes, peak effect in 10 to 15 minutes, and duration ranges from 2 to 3 hours. Hydromorphone is less hydrophilic than morphine, and its ability to penetrate the blood-brain barrier (BBB) is greater. It is approximately five times as potent as morphine and offers greater efficacy for patients with very severe pain. Hydromorphone also provides a good replacement for patients allergic or intolerant to morphine. Inpatients treated 24 to 72 hours with IV-PCA hydromorphone, who remain NPO or are just tolerating oral diet, may be transitioned to IV bolus doses (1 mg to 2 mg) of hydromorphone every 3 hours. The high concentration of hydromorphone solutions (2 to 4 mg/mL) also allow it to be administered subcutaneously with minimal patient discomfort.

Except for a ketone substitution, hydromorphone’s chemical structure and molecular weight are similar to morphine. Hydromorphone has a side effect profile similar to other opioids, including dose-dependent nausea, sedation, and respiratory depression. It appears to have a lower incidence of pruritus and excessive sedation than morphine.

Hydromorphone is primarily metabolized by hepatic glucuronidation. Drug accumulation and exaggerated effects can be expected in settings of hepatic and renal failure. However, its principal metabolite (hydromorphone-6-glucuronide) is inactive. For this reason, hydromorphone may be cautiously administered to patients with renal failure.

Oxymorphone (Opana IV)

Oxymorphone is a highly potent opioid analgesic that has been available for over 40 years. It is approved for surgical pain management and is currently available in a 1-mg vial. Oxymorphone has approximately ten times greater potency than morphine. Its onset to peak effect is more rapid than morphine and its overall analgesic efficacy is superior. Analgesic onset is noted within 5 minutes and the duration of effect can last 3 to 4 hours. Oxymorphone should be reserved for patients experiencing very severe pain in the PACU and surgical care units. Rather than spending considerable time titrating doses of morphine, 1 mg to 2 mg of IV oxymorphone can rapidly establish an effective level of analgesia for patients recovering from painful procedures and others with a high-grade opioid tolerance.
Controlled-release oxycodone preparations (Oxycontin) are available and offer prolonged (12 hours) and uniform analgesia, avoiding analgesic effects than oxycodone alone and include those containing acetaminophen (Percocet, Lortab) or ibuprofen (Combunox). Doses for surgical pain management are 5 mg to 15 mg every 4 to 6 hours. Compounds containing oxycodone provide greater doses in PACU reported less pain and need for supplemental opioids than others treated with equivalent doses of morphine. In a very large 3954 inpatient series, methadone was effective for patients suffering prolonged and very painful surgical- and medical-related acute pain.

Methadone (Dolophine)

Parenteral doses of methadone may be considered for patients with opioid tolerance and others suffering severe acute pain that is poorly responsive to morphine and hydromorphone. In acute pain settings, methadone doses of 0.25 to 0.3 mg/kg employed as monotherapy provide effective analgesia for up to 12 hours. Patients generally require little to no supplementation with IV-PCA opioids. Following lower abdominal surgery, patients treated with parenteral methadone 20 mg intraoperatively followed by PRN doses in PACU reported less pain and need for supplemental opioids than others treated with equivalent doses of morphine. In a very large 3954 inpatient series, methadone was effective for patients suffering prolonged and very painful surgical- and medical-related acute pain.

Methadone may also be employed as an adjuvant or as primary therapy. Adjuvant doses of 0.1 mg/kg or less every 12 hours provides useful augmentation of the analgesic effects provided by a primary opioid such as hydromorphone or oxycodone. Methadone is also advocated for patients suffering nerve injuries and neuropathic pain, as well as individuals who are highly opioid dependent or opioid hyperalgesic.

Methadone is associated with opioid-related side effects, including sedation, confusion, nausea, and vomiting, but unlike morphine and meperidine, it does not release histamine. Methadone blocks potassium channels expressed in myocardial cells. Therapeutic plasma levels are associated with prolongation of the Q-T interval and may initiate or exacerbate torsades de points and reentry arrhythmias. A screening EKG may be necessary to evaluate the Q-T interval when methadone doses exceed 60 mg/day.

Fentanyl (Sublimaze)

Fentanyl is employed in hypotensive patients or those with well-documented allergies to naturally occurring or semisynthetic opioids. Fentanyl is associated with minimal effects on cardiac output or blood pressure. Because of its hemodynamic stability, it is safer than morphine for use in patients with clinically significant cardiac and cerebral disease.

Doses of 50 mcg to 200 mcg are commonly administered to patients recovering from ambulatory surgery and provide rapid pain relief. Similar doses offer useful analgesia for patients requiring closed reductions and dressing changes.

IV infusions of fentanyl (0.5 to 5 mcg/kg/hour) may be used for sedation and pain control in ventilated or hemodynamically unstable patients. Infusion rates may be increased or diminished in response to inadequate pain control or to minimize adverse events. In addition, bolus doses of fentanyl (25 mcg to 50 mcg) or hydromorphone (0.5 mg to 1 mg) may be administered for breakthrough pain.

Oral Opioids

Morphine

Oral morphine remains the world standard for surgical pain management. Clinically, it has high analgesic potency, a slow onset to peak effect, and an intermediate duration of activity. Morphine’s delayed onset of analgesia has been related to the fact that it has difficulty penetrating the BBB. Morphine is poorly absorbed from the GI tract and doses are generally three times higher than that required parenterally.

Typical doses for postsurgical pain management are 20 mg to 40 mg every 4 to 6 hours. Morphine elixir may better tolerated than oral tablets in patients who have just been advanced to oral diet.

Oxycodone (Roxydalone, Oxycontin)

Oxycodone is a semi-synthetic µ and k receptor agonist that is commonly prescribed in the United States for postsurgical pain, and has high oral bioavailability because of rapid GI absorption and limited enterohepatic metabolism. In clinical practice, oxycodone does not release significant amounts of histamine and is associated with less sedation than equivalent doses of morphine. Oxycodone, like codeine and hydrocodone, is primarily metabolized through microsomal CYP3A4 and/or CYP2D6 pathways. Coadministration of medications that interact with these pathways may affect the plasma levels of oxycodone, resulting in reduced analgesia or adverse events. Up to 12% of oral oxycodone is demethylated and converted to oxymorphone, a highly potent opioid agonist.

Oxycodone is a versatile analgesic available as either an oral tablet, elixir (OxyIR), or compounded with acetaminophen. Typical doses for surgical pain management are 5 mg to 15 mg every 4 to 6 hours. Compounds containing oxycodone provide greater analgesic effects than oxycodone alone and include those containing acetaminophen (Percocet, Lortab) or ibuprofen (Combunox). Controlled-release oxycodone preparations (Oxycontin) are available and offer prolonged (12 hours) and uniform analgesia, avoiding
toughs of effect observed with IR oxycodone. When converting surgical patients from IV-PCA morphine to controlled-release oxycodone, calculate the prior 24-hour dose of morphine, then multiply by 1.5. One half of that amount is then given twice daily, with additional IR oxycodone 5 mg provided if requested (Table 7.2).30

Hydrocodone-Acetaminophen Compound
(Vicodin, Lortab)

Hydrocodone is a µ-selective opioid agonist that is commonly prescribed for inpatient and outpatient surgical pain management. This semi-synthetic derivative of codeine provides greater potency and analgesic efficacy, as well as improved tolerability, than the parent compound.2,24,26,30 The oral analgesic potency of hydrocodone is equivalent to oxycodone; however, many clinicians in the United States consider it to be a weaker drug with lower abuse potential. Compounded hydrocodone plus acetaminophen tablets, up to 15 mg and total 300 mg hydrocodone per day, are less controlled (schedule III) than other semisynthetic opioids and generally do not require triplicate prescriptions. This lower level of regulation, together with hydrocodone’s reliability in relieving moderate to severe pain, explains why it is so widely prescribed by surgical caregivers.2,24,26,30 Hydrocodone undergoes hepatic O-demethylation by CYP2D6 into the more potent opioid hydromorphone, which is eventually glucuronidated and excreted in urine.2,3 Patients who are extensive CYP2D6-hydrocodone metabolizers report greater analgesic benefits than poor metabolizers.2

Hydromorphone

Hydromorphone (Dilaudid) is a semi-synthetic, µ-selective opioid agonist developed over 80 years ago, and used for treatment of moderate to severe pain. It has an oral analgesic potency five to six times greater than morphine, and its onset of effect is more rapid.2,3,31,32 Oral doses of hydromorphone are associated with less histamine release than morphine and is less likely to precipitate hypotension and bronchoconstriction.2,3 In the United States, hydromorphone is often substituted for morphine in postsurgical settings. It is particularly useful in patients with severe pain unresponsive to morphine, and those who have had safe and effective pain control with IV-PCA or IV bolus doses of hydromorphone. It is also employed in individuals with high-grade opioid tolerance and patients suffering adverse events with oral hydrocodone or oxycodone.3,24 Hydromorphone is available as oral tablets and an oral elixer.

Oxymorphone (Opana IR, Opana ER)

Oxymorphone is a semisynthetic µ-selective opioid agonist.2,11 Oxymorphone has poor GI absorption and high enterohepatic metabolism. For this reason, its oral potency is only one tenth that of IV oxymorphine, and three times that of oral morphine.2,33 Oxymorphone is primarily metabolized by hepatic glucoronidation and not by CYP450 enzymes.2,33 It neither inhibits nor induces CYP450 pathways. These properties may offer clinical advantages over oxycodone and codeine for patients coadministered other medications metabolized by this pathway.2,21,31,33 Oxymorphone IR (Opana IR) is available as an oral tablet for moderate to severe acute pain.33 The analgesic effectiveness, safety, and tolerability of this preparation have been demonstrated in several postsurgical pain trials.33,34 Oxymorphone is also available as a sustained-release analgesic that provides a reliable 12-hour duration of effect (Opana ER).33 Sustained-release oxymorphone is not indicated for surgical pain unless it is expected to be very severe and of prolonged duration.33

Tapentadol (Nucynta)

Tapentadol was FDA approved in 2009 and is the first new analgesic for moderate to severe acute pain in more than 25 years. Tapentadol is a potent, dual-acting analgesic that combines central µ-opioid receptor agonism with monoamine reuptake inhibition to suppress pain transmission. Tapentadol offers analgesic efficacy comparable to classic opioids but with unexpectedly improved GI tolerability.35 The efficacy and safety of tapentadol IR compared with 10 mg to 15 mg oxycodone IR have been evaluated in several placebo-controlled postoperative pain trials.35,36 These trials demonstrated that tapentadol IR (50 mg) and oxycodone IR (10 mg) provide equivalent analgesia; however, a lower percentage of patients treated with tapentadol IR 50 mg reported nausea and/or vomiting (35% vs 59%; P<0.001) (Table 7.3). Tapentadol tablets can be given in doses of 50 mg, 75 mg, or 100 mg every 4 to 6 hours, depending on the pain intensity. The maximum daily dose is 700 mg (for the first day of treatment) and 600 mg (day 2 and after).

The analgesic activity of tapentadol is limited to the primary molecule, and no enzymes are needed to convert it to an active metabolite (as is the case with tramadol or codeine).35 This implies fewer, if any, individual variations in its action compared with opioids whose pharmacology is influenced by polymorphic enzymes. No dosage adjustment is needed in mild or moderate renal impairment. Little information exists regarding tapentadol dosing in opioid-dependent patients. Data taken from a 90-day safety trial in which some patients had been taking opioids prior to enrollment suggests that tapentadol doses of 100 mg every 4 hours may be appropriate.35 Like other opioid agonists, tapentadol is associated with nausea, vomiting, respiratory depression, and sedation; in addition, it may in rare situations precipitate serotonin syndrome. Serotonin syndrome is characterized by mental-status changes (eg, agitation, hallucinations, hyperreflexia) and autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia). The risk of serotonin syndrome is increased with concomitant administration of SSRIs, SNRIs, and MAOIs.35 Tapentadol has an abuse potential similar to hydromorphone and is subject to criminal diversion. After 90 days of continuous administration, abrupt discontinuation of tapentadol was associated with mild to moderate withdrawal symptoms in 17% of patients.35

Methadone (Dolophine)
Methadone is a synthetic phenylpropylamide-type opioid agonist with approximately 1.5 to 2 times the potency of morphine. Following oral administration, methadone is well absorbed, having a bioavailability that approaches 80%. It also has a large volume of distribution and a prolonged, yet variable (12 to 120 hours), plasma elimination half-life. Oral dosing of methadone is complicated and over- and underdosage is common. Despite its prolonged elimination half-life, methadone’s redistribution half-life and duration of effect are limited. Initial oral doses provide up to 6 hours of analgesia; however, as drug accumulates in tissue, analgesic duration and risk of overdosing may increase substantially. In addition to its activity at opioid receptors, methadone appears to provide additional analgesic effects via interactions with NMDA and α-adrenergic receptors.

Methadone is recommended for patients suffering postsurgical nerve injuries and neuropathic pain, as well as individuals who are highly opioid dependent or opioid hyperalgesic. Orally administered methadone is metabolized by the hepatic microsomal enzyme system undergoing N-demethylation or deamination into inactive compounds. Methadone is available as an oral elixir or oral tablets.

**Tramadol (Ultram)**

Tramadol is a weak μ-receptor opioid agonist with equivalent potency to codeine. Tramadol also has α-adrenergic analgesic effects that complement the opioid-mediated effect. It is not recommended for severe acute pain but is used for mild to moderate discomfort following minor surgery. In acute pain settings, doses of tramadol should not exceed 300 mg/day and it should not be prescribed to patients taking MAOIs as it may induce psychotic behavior. Tramadol also inhibits serotonin reuptake and can cause serotonin syndrome. Tramadol is metabolized by CYP2D6 into an active metabolite that has 200 times greater μ-receptor affinity and has five times greater potency than the parent compound. Like codeine, approximately 20% of individuals have CYP2D6 enzyme polymorphisms that result in poor metabolism. These patients cannot form the active metabolite and are at increased risk for analgesic failure.

**Meperidine (Demerol)**

Meperidine is weak synthetic opioid agonist with an oral potency equivalent to one tenth that of morphine. Its analgesic onset is slightly more rapid than morphine, however, its duration of effect is only two thirds as long. Meperidine was initially developed as an anticholinergic and provides a smooth muscle-relaxing effect. Oral doses exceeding 1 g/day or administration to patients with renal failure may result in neurotoxicity secondary to the accumulation of its neurotoxic metabolite, normeperidine. In addition, meperidine elevates serotonin levels and can precipitate a serotonergic crisis when coadministered with drugs that elevate serotonin, such as MAOIs. Meperidine tablets are increasingly restricted in hospital settings and should never be considered for chronic pain management.

**Fentanyl (Sublimaze)**

Fentanyl is a synthetic, μ-specific opioid agonist related to meperidine. Oral doses are potent (25 to 40 times greater than morphine), have a rapid onset, and 60- to 90-minute duration of effect. Fentanyl’s side effect profile is lower than that observed with morphine; however, dose-dependent nausea, sedation, and pruritus are commonly observed. Major adverse effects include rapid and profound respiratory depression and severe nausea and vomiting. Fentanyl is available as a transdermal patch and a transmucosal oral lozenge (Actiq orale). Approximately 30% of analgesic effect provided by the oral lozenge is via direct absorption through the oral mucosa. None of these preparations are approved for postsurgical pain management. However, fentanyl orale may be considered for patients with breakthrough pain who cannot tolerate oral opioid tablets.

**Codeine**

Codeine is a naturally occurring opiate-derived analgesic that is one fourth to one third as potent as morphine. Oral doses of codeine are used primarily in patients recovering from dental and ENT surgery. Its analgesic efficacy is inferior to oxycodone, while its side effect profile, particularly nausea and vomiting, is higher. Codeine is a pro-drug that must be metabolized to morphine by CYP2D6 to achieve analgesic effect. This enzyme is polymorphic, however, most patients are rapid or intermediate metabolizers. Approximately 20% of individuals are poor metabolizers who have a high incidence of analgesic failure. Others who are extensive metabolizers are at increased risk for morphine-related adverse effects, including excessive sedation and respiratory depression. Codeine is available as an oral tablet compounded with acetaminophen (Tylenol #3) that offers no analgesic advantages over compounded oxycodone or hydrocodone.

**Buprenorphine (Subutex, Suboxone, BuTrans)**

Buprenorphine is a partial agonist-type opioid that has been widely used as an IV analgesic in the European Union. Buprenorphine has a high μ-receptor affinity and occupation rate, and for this reason, greater than normal doses of agonists or antagonists are required to displace it and reverse its effects. A sublingual formulation of buprenorphine (Subutex) and buprenorphine plus naloxone (Suboxone) are increasingly used as maintenance therapy for opioid-dependent patients and for pain management. Patients presenting for surgery should continue taking these formulations during the perioperative period as both can provide effective pain control. Additional pain control can be provided with a fentanyl infusion, fentanyl lozenge, regional techniques, and the use of nonopioid analgesics. Alternatively, patients treated with buprenorphine can be converted to 30 mg to 40 mg of methadone/day 1 week prior to surgery to prevent withdrawal and to avoid antagonism of standard opioid analgesics.
A new transdermal buprenorphine formulation (BuTrans) which provides a 7-day duration of effect is available for chronic mild to moderate pain. Presently transdermal buprenorphine is not approved for surgical pain management, and whether it should be continued perioperatively has not been determined.

A list of opioid analgesics commonly used for postoperative pain management and recommendations for dose conversion are outlined in Table 7.4.

**Future Directions With Oral and Parenteral Opioids for Postsurgical Pain**

In the near future, improved and more selective opioid analgesics may be developed that better suit individual patient needs:

- Rapidly disintegrating and readily absorbed lingual and buccal preparations avoid gastric absorption and first-pass hepatic metabolism, and offer advantages of convenience and rapid analgesic onset. While originally developed for breakthrough chronic pain, these routes of delivery may become available for acute pain management. Nasal- and pulmonary-delivered opioid preparations offer similar advantages as well as convenience, and may displace the need for IV dosing and possibly IV-PCA in patients who remain NPO.
- Improved formulations may provide analgesic potentiation, lower incidence of adverse events, and opioid-sparing effects by developing opioid combinations (morphine plus oxycodone) or compounding opioids with either α2 agonists (tapentadol-like drugs) and α2-δ antagonists such as pregabalin.
- Opioids with a lower risk of diversion and abuse. Opioids formulated in crush-resistant, water-insoluble tablets may provide a lower risk for diversion, adulteration, and abuse (snorting, injecting). Tablets containing mixtures of an agonist plus an antagonist that is released if the tablet is adulterated are also being studied.

**REFERENCES**


44. James IG, O’Brien CM, McDonald CJ. A randomized, double-blind, double-dummy comparison of the efficacy and tolerability of low-dose transdermal buprenorphine (BuTrans seven-day patches) with buprenorphine sublingual tablets (Temgesic) in patients with osteoarthritis pain. *J Pain Symptom Manage.* 2010;40(2):266-278.

TABLE 7.1 — Oral Opioid Analgesics and Intravenous

**Benefits**
- Rapid onset of analgesia for moderate, severe, and very severe pain
- Highly effective analgesia (no analgesic dose ceiling)
- Selective analgesia:
- Reductions in pain suffering –
- Minimal effects on pain localization –
- No effects on key organs:
- Cardiac –
- Renal –
- Hepatic –
- Hemostatic safety –
- Multiple agents and routes of administration are available
- Relatively inexpensive (morphine, oxycodone)

**Drawbacks**
- Annoying side effects:
- Nausea –
- Pruritus –
- Sedation –
- Constipation –
- Clinically significant effects:
- Ileus –
- Bowel obstruction –
- Severe vomiting –
- Confusion –
- Dysphoria –
- Life threatening effects:
- Airway obstruction –
- Respiratory depression –
- Respiratory arrest –
- Social effects:
- Dose escalation –
- Physical dependence –
- Diversion and abuse –
- Addiction –
- May be expensive (sustained-release opioids, oral buccal preparations)

TABLE 7.2 — Oral Oxycodone CR in the Postoperative Setting

**Estimating the Initial Daily Dose of**

**Conversion Factors for**

<table>
<thead>
<tr>
<th>Conversion Factor</th>
<th>Prior IV Opioid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5</td>
<td>Morphine</td>
</tr>
<tr>
<td>0.2</td>
<td>Meperidine</td>
</tr>
<tr>
<td>10</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>200-300</td>
<td>Fentanyl</td>
</tr>
</tbody>
</table>

*The initial oxycodone CR dose was calculated according to the formulas:

- \( \text{oral oxycodone CR dose (mg/day)} = \text{Prior IV opioid (mg/day)} \times \text{conversion factor} \)
- \( \text{initial oral oxycodone CR dose (mg q12h)} = \text{Oral oxycodone CR dose (mg/day)} / 2 \)

TABLE 7.3 — Percentages of Patients Experiencing Nausea and Vomiting in Randomized, Double-Blind, Placebo-Controlled Studies of Tapentadol IR

<table>
<thead>
<tr>
<th>IR Oxycodeone HCl</th>
<th>100 mg</th>
<th>75 mg</th>
<th>50 mg</th>
<th>Placebo</th>
<th>Adverse Event (10 or 15 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>67</td>
<td>49</td>
<td>38</td>
<td>35</td>
<td>13</td>
<td>Nausea Bunionectomy</td>
</tr>
<tr>
<td>42</td>
<td>32</td>
<td>21</td>
<td>18</td>
<td>3</td>
<td>Vomiting</td>
</tr>
<tr>
<td>41</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>53</td>
<td>*53 Nausea and/or vomiting</td>
</tr>
<tr>
<td>70</td>
<td>Bunionectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a* The initial oxycodone CR dose was calculated according to the formulas:

- \( \text{oral oxycodone CR dose (mg/day)} = \text{Prior IV opioid (mg/day)} \times \text{conversion factor} \)
- \( \text{initial oral oxycodone CR dose (mg q12h)} = \text{Oral oxycodone CR dose (mg/day)} / 2 \)

*b* Vomiting
### TABLE 7.4 — Dosing Guidelines for Oral and Parenteral Opioids

<table>
<thead>
<tr>
<th>Dose</th>
<th>Route</th>
<th>Opioid (mg)</th>
<th>Comments</th>
<th>Duration</th>
<th>Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histamine release</td>
<td>3.5-4 hr</td>
<td>10 min</td>
<td>10 (5-15)</td>
<td>IV</td>
<td>Poor oral effect, active metabolite</td>
</tr>
<tr>
<td>Morphine</td>
<td>4-5 hr</td>
<td>45 min</td>
<td>30 (15-45)</td>
<td>PO</td>
<td>Morphine</td>
</tr>
<tr>
<td>Useful for visceral pain</td>
<td>4 hr</td>
<td>3 hr</td>
<td>10 min</td>
<td>100 (75-125)</td>
<td>IV Toxic metabolite</td>
</tr>
<tr>
<td>Meperidine</td>
<td>3.5 hr</td>
<td>45 min</td>
<td>200 (1-300)</td>
<td>PO</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Similar to oxycodone</td>
<td>4-6 hr</td>
<td>3 hr</td>
<td>30 min</td>
<td>10 (5-15)</td>
<td>PO Hydrocodone</td>
</tr>
<tr>
<td>Good oral analgesic</td>
<td>4-6 hr</td>
<td>3 hr</td>
<td>30 min</td>
<td>100 (75-125)</td>
<td>PO Oxycodone</td>
</tr>
<tr>
<td>High side-effect profile</td>
<td>3.5 hr</td>
<td>3.5 hr</td>
<td>45 min</td>
<td>50 (30-70)</td>
<td>PO Codeine</td>
</tr>
<tr>
<td>Prolonged elimination</td>
<td>6-8 hr</td>
<td>10-20 min</td>
<td>(7.5-15)</td>
<td>PO</td>
<td>Methadone</td>
</tr>
<tr>
<td>Difficult to titrate</td>
<td>6-8 hr</td>
<td>5-10 min</td>
<td>1.5-7.5 (5-10)</td>
<td>IV</td>
<td>Methadone</td>
</tr>
<tr>
<td>Well tolerated severe pain</td>
<td>3.5-4 hr</td>
<td>10-15 min</td>
<td>2 (1-3)</td>
<td>15 (7.5-15)</td>
<td>PO Hydromorphone Useful for</td>
</tr>
<tr>
<td>Poor oral bioavailability</td>
<td>4 hr</td>
<td>5-6 hr</td>
<td>30 min</td>
<td>10 (5-15)</td>
<td>PO Oxymorphone Useful for severe pain</td>
</tr>
<tr>
<td>IV Fentanyl (Oralet)</td>
<td>200-1200 mc</td>
<td>5-10 min</td>
<td>120 Rapid onset min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>100 (1-200)</td>
<td>40 min</td>
<td>4-6 hr</td>
<td>For mild-to-moderate pain</td>
<td></td>
</tr>
</tbody>
</table>

Values listed represent approximations based on single dose calculations. According to this conversion scheme, IV morphine is assigned a potency of “1” while oral morphine is considered 0.3 due to its poor bioavailability and higher dose requirement. Methadone values represent single-dose effects, accumulation of drug and duration of action will increase with continued dosing.

To calculate oral-to-oral dose conversions, determine the prior 24-hour opioid dose (both scheduled and rescue doses) then utilize opioids according to the PO equianalgesic dose and potency listed above. Utilize the following proportion: “Potency of current opioid” over “24-hour dose of current opioid”, multiplied by “potency of new opioid” over “X”. Solve for X by cross multiplication. X equals the 24-hour dose of the new drug. Divide the 24-hour dose and administer into increments according to the duration of action of the new drug.

For patient safety, consider using ½ to ⅓ less drug than the amount calculated. To calculate approximate IV-to-PO equianalgesic dose, utilize the table and multiply the potency of the currently used IV opioid by the prior 24-hour dose in mg. Divide this value by the potency of the PO opioid to which the patient will be converted. This value is administered in divided doses based on the duration of the PO opioid. To provide greater patient safety, divide this calculated dose by ½ to ⅓ and gauge its effectiveness. Subsequent dosing may be increased or decreased as necessary.