Part III. Opioids for Perioperative Pain

Opioids serve as the cornerstone for severe acute postoperative pain management with proven efficacy for this indication. Nevertheless, patients must be counseled on the limited effectiveness of any analgesic in eliminating pain entirely. A balanced, rational multimodal analgesic approach, including use of non-pharmacologic modalities, is most effective in controlling pain while at the same time, minimizing analgesic doses and their resultant side effects that interfere with rehabilitation. Patient counseling and expectation management with emphasis on safety and functional goals are necessary components of a successful treatment plan. Patients on chronic opioid analgesic therapy (COAT) who are undergoing elective surgeries present challenges for both perioperative pain management and risk mitigation. For this reason, it is important to balance patients’ risks for both severe postoperative pain and opioid side effects. The following recommendations are intended to help manage patients’ pain and minimize risk associated with perioperative opioid use.

The goal of opioid therapy is to prescribe the briefest, lowest dose and least invasive regimen that minimizes pain and avoids dangerous side effects.2-5

Preoperative Period

Clinical Recommendations

1. Conduct a thorough preoperative evaluation, including history and physical:
   a. Ask about past and current use of, response to and preferences for analgesics.
   b. Check the Prescription Monitoring Program (PMP). While this is especially important for patients with a history of COAT or benzodiazepine or sedative-hypnotic use, it is a best practice to check the PMP when possible in every patient pre-operatively.
   c. Assess risk for potential postoperative opioid over-sedation and/or respiratory depression (Table 1) and difficult postoperative pain control (Table 2).
   d. Inform the entire perioperative team of the results of this risk assessment.
   e. Consider consultation with a specialist for “at risk” patients (e.g. pain management, addiction medicine, and/or behavioral health), particularly in patients at risk for both over-sedation (Table 1) and difficult postoperative pain control (Table 2).

2. Develop a coordinated treatment plan, including a procedure-based timeline for tapering opioids perioperatively (e.g., Table 3). Identify which provider will be responsible for managing postoperative pain including prescribing opioids:
   a. Generally, in opioid naïve patients, any opioids prescribed during the first 6 weeks postoperatively should be managed solely by the surgeon.
b. If a patient was previously using chronic opioids for the condition being addressed by surgery, the surgeon should consult with the outpatient prescriber as to whether or not the patient is likely to need continued COAT after surgery. If so, develop a plan for transition of pain care back to the outpatient prescriber.

c. In the immediate postoperative period, during the hospital stay, the surgeon (or a specialist consultant) should manage all pain medication, including chronic methadone, buprenorphine/naloxone, or other COAT, as well as any additional opioids added for acute postoperative pain. These acute post-surgical opioids should be tapered-off according to the procedure-specific evidence-based guidance (e.g., Table 3). Continuation of previous COAT upon hospital discharge should be the responsibility of the outpatient prescriber.

3. Inform patient and family of the perioperative pain plan. Set expectations with them about realistic pain management goals, including functional recovery activities, need for multimodal treatment, limits of therapy, and the timeline (e.g., Table 3) for tapering off of opioids for the opioid naïve patient and back to preoperative opioid dose or lower in COAT patients.

4. Avoid new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics, or other central nervous system (CNS) depressants.

5. Avoid escalating opioid doses before surgery. The lowest effective dose should always be sought, but there is insufficient evidence to recommend routinely lowering chronic opioid doses or discontinuing opioids prior to surgery.

Intraoperative Period

Clinical Recommendations

1. Provide balanced multimodal analgesia, including adjuvant analgesics, when possible (e.g. acetaminophen, NSAIDs, gabapentin and local anesthetic infiltration). Under specialist direction, intravenous ketamine or lidocaine, and regional local anesthetic techniques can also help minimize perioperative opioids and their side effects.

2. Provide sufficient intraoperative opioid doses to avoid acute withdrawal in patients who are on high doses of preoperative opioids.

Immediate Postoperative Period

Clinical Recommendations

1. Always prescribe NSAIDs and acetaminophen or both for pain as a first-line analgesic (scheduled) unless contraindicated and encourage use of non-pharmacologic strategies as part of a multimodal “as needed” analgesic regimen.

2. Reserve the use of opioids for moderate to severe acute pain. If used, utilize the lowest possible dose as part of a multimodal regimen, including NSAIDs, acetaminophen, and non-pharmacologic therapies, unless contraindicated.

3. If using opioids, refer to Table 1 for recommended ranges for numbers of tablets to provide in a prescription based on evidence that the majority of patients will need only a limited number of
tablets based on the invasiveness of the procedure performed. While pain may persist for weeks following some surgeries, pain severe enough to warrant ongoing opioid use after several days requires reevaluation.

2.4. Counsel patients on the risks of opioids, to use opioids at the lowest effective dose and to stop using opioids as soon as possible. For example, use statements such as:

a. “Opioids are strong pain medications that can cause severe side effects including slowing your breathing causing your heart to stop and changes in your brain resulting in addiction.”

b. “The safest way to use opioids is to use the smallest dose for the shortest time period and to take opioids only to treat severe pain.”

c. “I expect you to not require opioids to treat your pain within a week”

d. “You should not continue to take these medications once your pain is manageable without them”.

3.5. Provide information about safe storage of opioids during use and disposal once opioids are no longer being used.

4.6. Monitor sedation and respiratory status in patients receiving systemic opioids for postoperative analgesia (e.g. Richmond Agitation Sedation Scale, Ramsey Sedation Scale, or Comfort Scale). Due to the risk of excessive sedation and respiratory depression, patients should be monitored closely in the initial hours following surgery and with subsequent dose escalations. Monitoring should include assessments of alertness and signs or symptoms of hypoventilation or hypoxia:

a. The use of routine oxygen is discouraged as hypoxia is a late sign of respiratory compromise and this sign will be delayed still further by supplemental oxygen.

b. There is insufficient evidence to recommend the routine use of more sophisticated noninvasive methods (such as capnography) for monitoring hypoventilation postoperatively.

c. Providers should be prepared to change or reduce opioids or administer opioid antagonists in patients who develop excess sedation or respiratory depression (Table 2).

5.7. Use oral opioids for managing postoperative pain in patients who can tolerate oral medications, particularly following the first or second postoperative day, as pain levels at rest and during activity become less variable.

a. Consider the use of patient controlled analgesia (PCA) initially in cases where repeated doses of parenteral opioids are anticipated or required. Providers should be aware of the doses being self-administered by their patients via PCA to guide adjustments. Routine use of continuous opioid infusions (basal rates with PCA) is NOT recommended:

b. Consider consultation with specialists for patients receiving high dose PCA, and when benzodiazepines, sedative-hypnotics or other opioids, are being used in combination with PCA.

6.8. Use short-acting “as needed” (PRN) opioids as the foundation for acute severe postoperative pain in the opioid naïve patient. For the opioid tolerant patient, do not add or increase extended release or long-acting opioids in the immediate postoperative period.
a. Avoid therapeutic duplication of opioids consisting of more than one type of PRN short-acting opioid (e.g., oxycodone and morphine). Avoid co-administration of parenteral and oral PRN opioids for ongoing pain. If PRN opioids from different routes are needed, provide a clear indication for when to use each route (e.g., intravenous opioids for brief, severely painful, closely monitored procedures such as dressing changes).

b. Consider scheduling non-opioid analgesics (e.g., acetaminophen or NSAIDs) for more steady analgesia and to avoid multiple PRNs for pain.

2.9 Resume pre-operative analgesic regimen as soon as possible if patients were previously on chronic opioids and are expected to continue these postoperatively.

8.10 Avoid new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics or CNS depressants. If patients were previously on chronic sedatives, restart these at lower doses (e.g., 50%) in the setting of postoperative opioids to avoid synergies between CNS depressant and opioid side effects.

9.11 Initiate a bowel regimen as soon as possible postoperatively to minimize opioid-induced bowel dysfunction (constipation). This side effect may still require opioid dose reductions if unresponsive to stool softeners, laxatives or enemas.

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- Post-operative opioid dosing shall, in most cases, follow the evidence-based guidance in Table 1.
- The rationale for exceptions should be well documented in the record.
- Continued opioid therapy will require appropriate re-evaluation by the surgeon, to assess and address problems with patient’s recovery that might be causing extended pain (e.g., dry socket after tooth extraction, slippage or re-fracture after an ortho surgery).
- If extended opioid therapy is required, this should be managed the same way as initiation of chronic opioid therapy including screening for misuse and education about risks and benefits.

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At Time of Hospital Discharge

Clinical Recommendations

1. Inform the patient and family which provider will be responsible for managing postoperative pain (usually the surgeon), including who will be prescribing any opioids. Instruct the patient and family on the planned taper of postoperative opioids, including a timeline for return to preoperative or lower opioid dosing for those on chronic opioids (e.g., Table 3).

2. Avoid continuing or adding new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics or CNS depressants. Counsel patients and families about risks of using alcohol and other CNS depressants with opioids.
3. Remind the patient of the dangers of prescription opioid diversion and the importance of secure storage of their medications. Sharing medications with others is never appropriate and is illegal. Instruct the patient and family on prompt disposal of controlled substances either through a DEA-approved pharmacy take-back kiosk or law enforcement site (www.takebackyourmeds.org) or following FDA guidelines for safe disposal of medications (e.g., flushing).

4. Follow through with the agreed upon pre-operative plan to taper off peri-operative opioids (e.g., Table 3) as surgical healing takes place. The goal is always the shortest duration and lowest effective dose:
   
   a. Most patients with major surgeries should be able to be tapered to preoperative doses or lower within **14 days** (and often <7 days) - depending on the invasiveness of the surgery (see Table 3). It is important to remember that for some minor surgeries, pain can often be managed with only acetaminophen or NSAIDs in conjunction with non-pharmacological therapies (e.g., heat or ice) with no or only a very limited supply of short-acting opioids (e.g. <3 days) - even if they were taking opioids preoperatively.
   
   b. For patients who were not taking opioids prior to surgery, but who are still on them after 6 weeks, follow the AMDG recommendations for Subacute Pain Opioid Prescribing.

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**Table 1. Risks for Over-sedation and/or Respiratory Depression from Postoperative Opioids**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep apnea or high risk sleep disorder (morbid obesity/history of snoring/positive STOP Bang score ≥4)</td>
<td>151-160</td>
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<tr>
<td>Age (&lt;1 and ≥65 years old)</td>
<td></td>
</tr>
<tr>
<td>History of over-sedation with opioids</td>
<td></td>
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<tr>
<td>Opioid analgesic tolerance or increased opioid dose requirement</td>
<td></td>
</tr>
<tr>
<td>Concurrent use of other sedating drugs (e.g. benzodiazepines, antihistamines, sedative/anxiolytics or other CNS depressants)</td>
<td></td>
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<tr>
<td>History of difficult to control postoperative pain</td>
<td></td>
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<tr>
<td>Long (&gt;6 hours) duration of general anesthesia</td>
<td></td>
</tr>
<tr>
<td>Surgery location and/or type (e.g. airway, upper abdominal, thoracic, scoliosis repair in children)</td>
<td></td>
</tr>
<tr>
<td>Medical comorbidities (e.g. pulmonary disease/smoker, cardiac disease, other major organ failures)</td>
<td></td>
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</tbody>
</table>

**Table 2. Risks for Difficult-to-control Postoperative Pain**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of severe postoperative pain</td>
<td>161-169</td>
</tr>
<tr>
<td>Opioid analgesic tolerance (daily use for months)</td>
<td></td>
</tr>
<tr>
<td>Current mixed opioid agonist/antagonist treatment (e.g. buprenorphine, naltrexone)</td>
<td></td>
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<tr>
<td>Chronic pain (either related or unrelated to the surgical site)</td>
<td></td>
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<tr>
<td>Psychological comorbidities (e.g. depression, anxiety, catastrophizing)</td>
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<tr>
<td>History of substance use disorder</td>
<td></td>
</tr>
<tr>
<td>History of &quot;all over body pain&quot;</td>
<td></td>
</tr>
</tbody>
</table>
Table 3. Duration of Opioid Treatment for Postoperative Pain

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Procedure Description</th>
<th>Opioid Prescription</th>
<th>Special Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents ≤ 24 years old</td>
<td>Dental extractions (e.g. third molar, wisdom tooth)</td>
<td>Prescribe ≤ 3 days (e.g., 8 to 12 tablets) of immediate release opioids in combination with acetaminophen and/or an NSAID for severe pain</td>
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</tr>
<tr>
<td>Adults</td>
<td>Dental extractions or simple oral surgery (e.g. graft, implant)</td>
<td>Prescribe ≤ 3 days (e.g., 8 to 12 tablets) of immediate release opioids in combination with acetaminophen and/or an NSAID for severe pain</td>
<td></td>
</tr>
<tr>
<td>Minor Invasive Procedures</td>
<td>Minor surgery (e.g. laparoscopic appendectomy, carpal tunnel release, laparoscopic cholecystectomy, breast biopsy, meniscectomy)</td>
<td>Prescribe ≤ 3 days (e.g., 8 to 12 tablets) of immediate release opioids for severe pain.</td>
<td></td>
</tr>
<tr>
<td>Moderately Invasive Procedures</td>
<td>Moderate surgery (e.g. rotator cuff repair, one-level laminectomy, vaginal or laparoscopic hysterectomy)</td>
<td>Prescribe ≤ 7 days (e.g., up to 42 tablets) of immediate release opioids in combination with acetaminophen and/or an NSAID for severe pain. Continued opioid use (refill) requires re-evaluation and documented need by surgeon.</td>
<td></td>
</tr>
<tr>
<td>Major Invasive Procedures</td>
<td>Major surgery (e.g. lumbar fusion, knee replacement, hip replacement, open abdominal surgery, thoracotomy)</td>
<td>Do not discharge with more than a 14-day supply of opioids in combination with acetaminophen and/or an NSAID. Continued opioid use (refill) requires re-evaluation and documented need by surgeon.</td>
<td>Taper off opioids within 6 weeks after surgery</td>
</tr>
<tr>
<td>Patients on Chronic Opioid Therapy</td>
<td>Elective major surgery in patients on chronic opioid therapy</td>
<td>Do not discharge with more than a 14-day supply of opioids in combination with acetaminophen and/or an NSAID. Continued opioid use (refill) requires re-evaluation and documented need by surgeon.</td>
<td>Resume chronic regimen if patients are expected to continue postoperatively; re-establish ongoing pain management care</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Taper opioids to preoperative doses or lower within 6 weeks after surgery; assure referral/access to ongoing pain management care</td>
</tr>
</tbody>
</table>

Although a prescription may be written for frequent dosing intervals such as "prn every 4 to 6 hours", avoid dispensing a number of tablets that equals the total allowable maximum dosing. For example, 1-2 tablets prn every 4 hours would be equal to a maximum of 84 tablets in a week. A patient should be expected to need less frequent dosing as pain resolves and thus will likely need a significantly lower number of tablets (as little as half) for a specific timeline (e.g., 14 days).
Evidence

A number of reviews of the literature on perioperative pain treatment have been undertaken and published in the last few years, including those from the American Pain Society, the American Society of Anesthesiologists, the Department of Defense, the Veterans Administration, and the Washington State Department of Labor and Industries. These guidelines as well as a PubMed search for additional reviews of this topic in the last 5 years (560, excluding 32 reviews concerning a single surgical procedure) were used and combined with consensus opinions from the experts in the AMDG advisory group to formulate our final recommendations. For this amended review and set of recommendations, the primary focus was on pertinent articles which were published since 2014.

While there is concern regarding patients receiving adequate pain control, especially following major surgical procedures, recent literature suggests that the majority of opioid pain medication is not taken and left over post-operatively. Hill et al (Ann Surg, 2017) estimated the number of opioid doses required for 80% of patients receiving post op opioids for 5 procedures. Across these 5 procedures, only 34% of the opioid doses had been taken. These investigators then taught the surgical personnel at Dartmouth to reduce the number of pills prescribed—the amount prescribed after this education was approximately 50% reduced, to a median of 5-15 pills across the 5 procedures.

The problem of post-op overprescribing may be even more problematic in children and adolescents. Voepel-Lewis et al, (JAMA Peds, 2015) estimated the number of opioid doses prescribed and left-over by parent diary on post-op day 4: For T&A, 52 pills dispensed, 44 pills left over; for musculoskeletal procedures, 34 pills dispensed, 30 pills left over, and for minor abdominal GU, and peripheral procedures, 31 pills dispensed, 28 pills left over. As pointed out in the Bree/AMDG dental opioid guideline (Ref), left over pills may be particularly risky in this vulnerable population; high schoolers who received one prescription of an opioid were 33% more likely to misuse opioids non-medically between 18-23 years (Mieche et al, Pediatrics, 2015). The problem of overprescribing in children and adolescents may also be contributing to the dramatic increase in heroin initiation in WA and elsewhere; the demographic with the largest increases in heroin deaths are in the 18-30 year age group.

New persistent opioid use is common after surgery. In a nationally representative sample, Brummet et al (JAMA Surg 2017) reported that postoperative opioid use beyond 90 days post-operatively occurred in 5.9-6.0% of patients who were opioid free for the year prior to surgery, with no significant difference in new persistent opioid use after minor and major surgical procedures. Persistent use occurred in nearly 8% of patients after carpal tunnel syndrome, and in over 10% of patients after colectomy. Using similar methods, the same University of Michigan group reported new persistent opioid use after 13 procedures in 4.8% of 13-21 year olds (Harbaugh et al, Pediatrics, 2018); the highest rates were seen in adolescents following...
colectomy (15.2%) and cholecystectomy (7.3). New persistent opioid use following surgery is significant in that much longer term use is highly likely. Martin *et al* reported that >50% of patients on opioids for 90 days would still be taking opioids years later (*Martin et al, JGIM, 2011*). More recently, Shah *et al* found that the likelihood of being on opioids for 1 year increases by 1%/day for each day starting with day 3 of the first prescription (*Shah et al, MMWR, 2017*). It is highly likely that meaningful dependence may develop after only days to weeks of opioid use to explain these observational study results. Using a large commercially insured population, Brat *et al* (BMJ 2018) conducted a nationwide assessment of risk of developing opioid dependence, abuse, or overdose among opioid-naive patients postoperatively. Total duration of opioid use was the strongest predictor, with each refill and additional week of opioid use associated with an (adjusted) rate of adverse outcome of 44%.

Although opioids are effective for short-term pain relief following surgery, side effects may limit their use. The use of a multimodal approach including non-pharmacologic interventions to manage pain can improve treatment and limit side effects from any one class of analgesics. Preparation for surgery such as training in relaxation, counseling and education can reduce anxiety, postoperative opioids use and physical therapy needs. In addition, adjuvant treatments such as acetaminophen, NSAIDs and gabapentin have been demonstrated to be opioid-sparing and help minimize opioid-related side effects. The intraoperative use of techniques such as local anesthetic blocks, ketamine and intravenous lidocaine can also reduce opioid requirements.

It is important to assess patients' risk factors for over-sedation and/or respiratory depression and for difficult-to-control postoperative pain. Predictors of postoperative opioid over-sedation and/or respiratory depression include, but are not limited to, sleep apnea, concurrent use of benzodiazepines or other CNS depressant agents, other medical conditions that affect respiratory function and prolonged anesthesia. Risk factors for difficult to control postoperative pain include chronic pain, mental health comorbidities (e.g. anxiety, depression, catastrophizing) and history of substance use disorder.

Patients on COAT who are undergoing surgery are at increased risk for both of these complications. These patients have higher pain rating, manifest more anxiety and have frequent and more severe respiratory depressive episodes than opioid-naive patients.

The Prescription Monitoring Program provides an accurate picture of the patient's history of opioid, benzodiazepine, and other controlled substance use, which is especially helpful for planning perioperative pain management. It is important to collaborate across the care team (surgeon, anesthesiologist, pain management specialist, bedside nurses, treating provider and the patient) to formulate a postoperative pain management plan including risk factors and a timeline for weaning analgesics. Communication of this treatment plan, as well as realistic expectations concerning postoperative pain, is important for the patient, his or her family and the entire care team to help ensure appropriate treatment and avoid dangerous side effects.
The first 24 hours of opioid therapy is a significant period of risk for excess sedation and respiratory depression. Assessment of sedation level and monitoring for adequate ventilation and oxygenation allow for early response and intervention. When the parenteral route is needed beyond the first few hours after surgery, patient-controlled analgesia (PCA) is recommended and can add an element of safety as the sedated patient is less likely to continue to give themselves opioid doses. However, routine use of PCA is not recommended, as patients can usually resume oral analgesia within hours of the surgery. Analgesic effects of oral and intravenous opioids are comparable, so patients can be transitioned to oral opioids as soon as oral intake is tolerated. Concurrent, as needed use of intravenous and oral opioids increases the risk of side effects. Constipation is a common adverse effect of opioids and, if left untreated, could lead to bowel impaction. Initiate a bowel regimen as soon as possible postoperatively in those taking opioids to minimize opioid-induced bowel dysfunction.

References