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 is most effective in controlling pain while at the same time, minimizing analgesic doses and their resultant side effects that interfere with rehabilitation. Patients on COAT who are undergoing elective surgeries present challenges for perioperative pain management. For this reason, it is important to assess patients' risks for both severe postoperative pain and side effects of opioids. 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, least invasive and lowest dose 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 ~~, especially~~ for patients with a history of COAT or benzodiazepine or sedative-hypnotic use, it is a best practice to check in every elective patient pre-operatively. .
    c. Assess risk for potential postoperative opioid over-sedation and/or respiratory depression (Table 4) and difficult postoperative pain control (Table 5). Inform the entire perioperative team of the results of the risk assessment.
    d. Consider consultation with a specialist (e.g. pain management, addiction medicine, behavioral health), particularly in patients at risk for both over-sedation (Table 4) and difficult postoperative pain control (Table 5).
2. Develop a coordinated treatment plan, including a timeline for tapering perioperative opioids. Identify which provider will be responsible for managing postoperative pain and 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 evidence-based guidance in Table 1. ~~during the first few weeks after surgery~~. 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, timely return to preoperative baseline opioid dose (if any) or lower, and the analgesic tapering timeline.
4. Avoid new prescriptions of benzodiazepines, sedative-hypnotics, anxiolytics, or other central nervous system (CNS) depressants.
5. Avoid escalating the opioid dose 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.

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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, ketamine, 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. 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.
2. 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 4).

3. 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 opioids, benzodiazepines or sedative-hypnotics are being used in combination with the PCA.

4. 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 for 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 use (e.g. for a brief, severely painful, closely monitored procedure such as a dressing change).

   b. Consider scheduling non-opioids for more steady analgesia and to avoid multiple PRNs for pain.

5. Resume chronic regimen as soon as possible if patients were previously on chronic opioids and are expected to continue these postoperatively.

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

7. 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.

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, AND EXCEPTIONAL CASES SHOULD BE RE-EVALUATED AND OFFERED INFORMED CONSENT FOR CONTINUED OPIOID THERAPY. ~~Do not discharge the patient with more than a two week supply of opioids, and many surgeries may~~ require less. Continued opioid therapy will require appropriate re-evaluation by the

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TABLE1 Duration of Opioid Treatment for Postoperative Pain	
Adolescents ≤ 24 years old	
Dental extractions (e.g. third molar, wisdom tooth)	• Prescribe NSAID or combination of NSAID and acetaminophen for mild to moderate pain • Prescribe ≤ 3 days (8 to 12 tablets) of immediate release opioids in combination with an NSAID or acetaminophen for severe pain
Adults	
Minor Procedures	
Dental extractions or simple oral surgery (e.g. graft, implant)	• Prescribe NSAID or combination of NSAID and acetaminophen for mild to moderate pain • Prescribe ≤ 3 days (8 to 12 tablets) of immediate release opioids in combination with an NSAID or acetaminophen for severe pain
Minor surgery (e.g. hernia repair, laparoscopic appendectomy, carpal tunnel release, laparoscopic cholecystectomy, biopsy, meniscectomy)	• Prescribe non-opioid analgesics (e.g. NSAIDs, acetaminophen) and non-pharmacologic therapies • Prescribe ≤ 3 days (8 to 12 tablets) of immediate release opioids for severe pain
Moderate Procedures	
Moderate surgery (e.g. ACL repair, rotator cuff repair, discectomy, laminectomy)	• Prescribe non-opioid analgesics (e.g. NSAIDs, acetaminophen) and non-pharmacologic therapies • Prescribe ≤ 7 days (up to 42 tablets) of immediate release opioids for severe pain. Continued opioid use requires appropriate re-evaluation by the surgeon
Major Procedures	
Major surgery (e.g. lumbar fusion, knee replacement, hip replacement)	• Prescribe non-opioid analgesics (e.g. NSAIDs, acetaminophen) and non-pharmacologic therapies • Prescribe the lowest effective dose and shortest duration of immediate release opioids. • Do not discharge with more than a 14-day supply of opioids. Continued opioid use requires appropriate re-evaluation by the surgeon • Taper off opioids within 6 weeks after surgery
Patients on Chronic Opioid Therapy	
Elective major surgery in patients on chronic opioid therapy	• Prescribe non-opioid analgesics (e.g. NSAIDs, acetaminophen) and non-pharmacologic therapies • Prescribe the lowest effective dose of immediate release opioids for acute pain. • Resume chronic regimen if patients are expected to continue postoperatively • Taper opioids to preoperative doses or lower within 6 weeks after surgery

At Time of Hospital Discharge

Clinical Recommendations

1. 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.
2. Inform the patient and family which provider will be responsible for managing postoperative pain, 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.
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 take-back program or FDA guideline for safe disposal of medicine (or retail pharmacy chain kiosk, packet of Dispose Rx, etc) .
4. Follow through with the agreed upon preoperative plan to taper off opioids added for surgery 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 3, 7 or 14 days depending on the invasiveness of the surgery (Table 1) Abdominal and thoracic procedures may have greater post-op analgesia needs than other surgeries. In some cases, the pain may be neuropathic, requiring gabapentenoids or similar drugs, not opioids, which are not effective for neuropathic pain. ~~6 weeks (approximately 20% of dose per week although tapering may be slower in the 1st week or 10 days and then become much more rapid as healing progresses).~~

    ~~b.~~a. It is important to remember that for some minor surgeries, particularly in adolescents <24 years, it is~~may be~~ appropriate to discharge patients on acetaminophen or NSAIDs only or with only a very limited supply of short-acting opioids (e.g. 2-3 days) - even if they were taking opioids preoperatively.

    ~~c.~~b. For patients who were not taking opioids prior to surgery, but who are still on them after 6 weeks, follow the recommendations in the Subacute Phase .

Table 1. Risks for Over-sedation and/or Respiratory Depression from Postoperative Opioids [151-160]

Sleep apnea or high risk sleep disorder (morbid obesity/history of snoring/positive STOP Bang score ≥4)
Age (<1 and >65 years old)
History of over-sedation with opioids
Opioid analgesic tolerance or increased opioid dose requirement

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Concurrent use of other sedating drugs (e.g. benzodiazepines, antihistamines, sedative/anxiolytics or other CNS depressants)
History of difficult to control postoperative pain
Long (>6 hours) duration of general anesthesia
Surgery location and/or type (e.g. airway, upper abdominal, thoracic, scoliosis repair in children)
Medical comorbidities (e.g. pulmonary disease/smoker, cardiac disease, other major organ failures)

Table 2. Risks for Difficult-to-control Postoperative Pain [161-169]

History of severe postoperative pain
Opioid analgesic tolerance (daily use for months)
Current mixed opioid agonist/antagonist treatment (e.g. buprenorphine, naltrexone)
Chronic pain (either related or unrelated to the surgical site)
Psychological comorbidities (e.g. depression, anxiety, catastrophizing)
History of substance use disorder
History of "all over body pain"
History of significant opioid sensitivities (e.g. nausea, sedation)
History of intrathecal pump use or nerve stimulator implanted for pain control

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 naïve patients post-operatively. 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. [170] 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. [171-184] Preparation for surgery such as training in relaxation, counseling and education can reduce anxiety, postoperative opioids use and physical therapy needs. [185-189] In addition, adjuvant treatments such as acetaminophen, NSAIDs and gabapentin have been demonstrated to be opioid-sparing and help minimize opioid-related

side effects. [184,190-192] The intraoperative use of techniques such as local anesthetic blocks, ketamine and intravenous lidocaine can also reduce opioid requirements. [193-195]

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. [151,156,157,159,160] 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. [161-165,167]

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 naïve patients. [162-165,196]

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. [197,198] 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. [199]

The first 24 hours of opioid therapy is a significant period of risk for excess sedation and respiratory depression. [159] Assessment of sedation level and monitoring for adequate ventilation and oxygenation allow for early response and intervention. [158,159,200-204] 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. [205-207] 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. [208] Concurrent, as needed use of intravenous and oral opioids increases the risk of side effects. [209] 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. [210,211]

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