

PAIN

Assessment and Recognition of Pain

The level of pain reported by the patient should be considered the “gold standard” for both initial evaluation as well as response to analgesia.¹ However, the ability to consistently and systematically achieve adequate pain control is enhanced by utilizing quantifiable pain scales, particularly in the ICU setting where verbal communication is frequently hindered. These objective scales help to avoid the error of assuming “sedation equals analgesia.”

Pain scales

For patients who can appropriately indicate pain, several one-dimensional reporting scales are available to evaluate the intensity of pain and the change in pain in response to intervention including the visual analog scale (VAS), the verbal rating scale (VRS), and the numeric rating scale (NRS) (Figure 1). The VAS is a well validated tool that utilizes a single horizontal line along, with “no pain” on the left end and “worst pain imaginable” on the right end, while the NRS uses a numeric scale of 0 through 10 to help patients rate their pain (“no pain” to “worst imaginable”). The NRS has the advantage of allowing both verbal and non-verbal documentation while providing a quantifiable number for assessment and compliance monitoring.

Objective findings

In the sedated, delirious, and/or intubated patient, physicians must often rely on objective clinical findings to guide care and analgesic administration. Tachycardia, hypertension, and tachypnea have traditionally been recognized as evidence of patient discomfort and pain. However, physiological signs have not shown reliable correlation with pain and

may greatly underestimate its presence; less than one-third of pain events are associated with abnormal vital signs in post-operative patients. Thus, the evaluation of both subjective “pain-related behaviors” (body movement, facial expressions) and objective parameters are often necessary.

Pharmacologic Management of Pain

Opiates

Opiates are the most common agents used for analgesia in the surgical patient and remain the gold standard against which all others are measured (Table 1). Opiates work through both central and peripheral opioid receptors, with the mu and kappa receptors having the most analgesic effects. The other receptors (sigma, delta, lambda) contribute to the majority of their adverse effects (respiratory depression, hypotension, urinary retention, ileus, and pruritus). Respiratory depression may occur with all members of this class at higher dosing ranges and is more frequently observed when combined with benzodiazepines. Hypotension may occur after opiates as a result of reversal of endogenous catecholamine effects on vascular smooth muscle constriction. Thus, hypotension after opioid administration is more common in the patients with hypovolemia or in those already demonstrating cardiovascular collapse (morphine, codeine, and meperidine).

Morphine: Morphine is the most commonly prescribed of the opioid analgesics as it is well known, inexpensive, and has an excellent analgesic effect. It has a long duration of action allowing intermittent dosing to achieve adequate pain control. Morphine does, however, have several active metabolites that require renal clearance and its use in

patients with renal failure increases the risk of toxicity and adverse event. In addition, morphine is associated with histamine release causing an associated pruritus.

Fentanyl: Fentanyl has a very rapid onset and a short duration, making intermittent dosing of fentanyl for continuous pain control problematic. It may be given to those with morphine allergies and does not cause histamine release. It does not have active metabolites requiring renal clearance and can be used safely in those with renal failure without dose adjustment. Fentanyl has been shown to demonstrate tachyphylaxis in chronic exposure which may require significant increasing in dosing requirements or even change to other agents. Additionally, fentanyl is extremely fat soluble and demonstrates accumulation within repeated dosing.

Hydromorphone: similar to morphine in its duration and onset, but lacks active metabolites and the histamine release often seen with morphine. As such, it may be used in those with hemodynamic concerns and renal insufficiency.

Meperidine: associated with significant side effect profile and should be avoided for the management of acute pain in the surgical patient. Meperidine has active metabolites that often lead to confusion, delirium, and even seizures. It may not be given by constant infusion or frequent intervals for this reason. Meperidine also interacts with many other medications, including MAO inhibitors and selective serotonin reuptake inhibitors.

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs provide analgesia through a non-selective, competitive inhibition of the cyclooxygenase (COX) enzyme, a critical component of the inflammatory cascade. Utilization of these medications may help reduce opioid requirements and is often adequate pain

control for musculo-skeletal pain (Table 2). Ibuprofen and ketorolac are the most commonly utilized oral and enteral forms of NSAIDs, respectively. However, NSAIDs are associated with gastrointestinal (GI) bleeding, platelet inhibition, and renal insufficiency. The adverse renal effects are more common in those patients who are hypovolemic, elderly, or receiving the medications for an extended period. Selective COX-2 inhibitors appear to be associated with less GI bleeding, but several have been withdrawn from the market by their manufacturers due to concern of increased risk of cardiovascular complications. Though widely used as an over-the-counter analgesic, aspirin is also associated with GI bleeding and platelet dysfunction. Therefore, its use as an analgesic in the acute setting is fairly limited.

Acetaminophen

Acetaminophen is often utilized as a primary medication for mild to moderate pain and as an adjunct in more severe pain. When combined with an opioid, the two medications achieve an analgesic effect much greater than with the opioid alone. Overdose and subsequent hepatotoxicity may occur when combination agents are not recognized as containing acetaminophen. Daily administration of the total acetaminophen dose should be limited to less than 4 grams (Table 2). However, both alcohol abuse and malnutrition lower the threshold for hepatotoxicity. Care must be taken to limit dosing to less than 2 grams in these patients.

Alpha-2 receptor agonists

Alpha-2 agonists (clonidine, dexmedetomidine) have been shown to be effective in primary and adjunctive control of pain and lack the side effect profile observed with opiates. These agents are relatively lipid soluble and absorbed and distributed fairly

quickly. Several mechanisms for their nociceptive effects have been debated, including spinal level inhibition of noradrenergic descending pathways and a reduction in pain perception.

Delivery options

Oral and Trans-dermal Delivery: The duration of analgesia and tolerance of adverse effects with oral forms of opioids makes the enteral tract the preferred administration route. In patients requiring frequent dosing, sustained release options are available but should only be administered orally (not through naso-gastric or naso-enteric routes). Fentanyl patches have shown adequacy in achieving pain control, but their use should be closely monitored and usually restricted to those with chronic pain issues.

Intravenous or epidural delivery: In patients requiring intravenous opioids, scheduled dosing (morphine, hydromorphone) or a continuous infusion (fentanyl, morphine) should be utilized to provide consistent analgesia. Though intermittent (as needed) regimens are often associated with inadequate pain control, excellent results (and superior patient satisfaction on pain scales) can be achieved through a patient-controlled analgesia (PCA) device. Therefore, if the patient is capable of operating such a device, a PCA, utilizing morphine or hydromorphone, should be employed. Neuraxial (epidural) anesthesia has been shown to achieve superior pain control following thoraco-abdominal procedures or trauma (rib fractures) compared to PCA. Epidural analgesia has also been shown to decrease nosocomial pneumonia rates and shorten duration of mechanical ventilation. Catheter placement, however, is associated with hypotension, dural puncture, spinal cord injury, and urinary retention.

***Acute Pain Management in Patients with Opioid Dependence: The analgesic properties of methadone and buprenorphine differ quite considerably from those utilized for acute pain. Additionally, tolerance and hyperalgesia associated with these agents likely diminishes any analgesic effect. Used alone, these agents usually prove grossly inadequate in providing acute analgesia. As well, cross-tolerance between these medications and other opioids may explain why this population often requires higher and more frequent doses of opiates. Management should focus on delivering uninterrupted therapy (to address baseline opioid requirements) and aggressive pain management strategies (to achieve acute analgesia). Similar to the managing opioid naïve patients, strategies should employ non-pharmacologic and non-opioid interventions as well. Though physicians are often concerned opioid administration in treating acute pain will result in relapse to active drug use, there is no evidence to support this bias.

Table 1. Opioids employed in the acute care of surgical patients

<i>Opioid</i>	<i>Initial dosing</i>	<i>Half-life</i>	<i>Renal dosing</i>	<i>Hepatic dosing</i>	<i>Adverse events</i>
Morphine	2-10 mg I.V. q2-6h	3-7 hr	Reduce by 25-50% if CrCL<50	Not defined	Histamine release
Fentanyl	25-100 mcg I.V. q 1-2h	1.5-6 hr	Reduce by 25-50% if CrCL<50	Not defined	Significant accumulation in fat, tachyphylaxis, rigidity with higher doses
Hydromorphone	0.2-0.6 mg I.V. q2-3 h	2-3 hr	Not defined	Not defined	Pancytopenia, agranulocytosis
Oxycodone	5-10 mg PO q4 hr	2-3 hr	Reduce by 25-50% if CrCL<50	Decrease initial dosing	Constipation, pruritus
Hydrocodone	7.5 mg PO q 4-6 hr	2-4 hr	Avoid with severe impairment	Avoid with severe impairment	Headache, pruritus
Methadone	2.5-5 mg PO q 8 hr	12 hr- 6 d	Reduce by 25-50% if CrCL<10	Decrease initial dosing	QTc prolongation, ventricular arrhythmias
Codeine	15-30 mg q4-6 hr	2-4 hr	Reduce by 25-50% if CrCL<50	Avoid with severe impairment	Constipation, pruritus

Table 2. Non-opioid options for acute pain control (primary and adjuncts)

	Initial dosing	Route of administration	Renal dosing	Hepatic dosing	Adverse events
Ibuprofen	600-800 mg q 6-8 hours	Oral	Avoid with renal insufficiency and hypovolemia; do not use with advanced renal disease	Not defined	Avoid in late pregnancy; gastrointestinal (GI) bleeding; perforation
Ketorolac	15-30 mg I.V., 30-60 mg I.M., or 10 mg P.O. every 6-8 hours	Intravenous, intramuscular, or oral	Avoid with renal insufficiency and hypovolemia; do not use with advanced renal disease	Not defined	For short-term use (<5days); GI bleeding, perforation
Celecoxib	200 mg every 12 hours	Oral	Avoid use with severe impairment	Decrease dose by 50% with Child-Pugh B; Avoid with Child-Pugh C	May increase risk of fatal cardiovascular thrombotic events (myocardial infarct, stroke)
Acetaminophen	325-650 mg every 4-6 hours	Oral	Adjust frequency with CrCL 10-50 to q 6; CrCL <10 to q 8	Limit use to 500 mg per dose and no more than 2000 mg/d	Do not exceed total acetaminophen dose of > 4000 mg/d
Aspirin	325-650 mg every 4 hours	Oral	Adjust frequency with CrCL 10-50 to q 6; Avoid with CrCL <10	Not defined	Do not exceed total aspirin dose of > 4000 mg/d