Advanced Concepts and Controversies in Emergency Department Pain Management

Sergey M. Motov, MD,*, Lewis S. Nelson, MD

INTRODUCTION

Pain is the most common complaint for which patients come to the emergency department (ED), with a prevalence of 45% to 75%. Pain managed in the ED may be acute and self-limited or chronic, and emergency physicians (EPs) have had to develop expertise in the management of a broad spectrum of acute and chronic painful conditions. Because poorly managed pain may cause significant behavioral, physiologic, and psychological distress, EPs must be well versed in the management of acute and chronic pain. Although the evidence-based management of acute pain is well characterized, the management of chronic pain is much less so, and much controversy exists. In this article, we address some of the more common advanced concepts and controversies in emergency department pain management.

KEYWORDS

- Acute pain
- Chronic pain
- Emergency department
- Pain management
- Opioids
- Nonopioid analgesics

KEY POINTS

- The key to successful parenteral opioid analgesia is the titration of these analgesics regardless of the initial dosing regimen.
- The greatest limitation to the use of intravenous (IV) versus oral acetaminophen is the nearly 100-fold cost differential, which is likely not justified by any marginal improvement in pain relief.
- The use of IV subdissociative dose of ketamine administered either alone or in combination with opioids is effective for the treatment of acute pain; however, it is associated with relatively high rates of minor, short-lived adverse side effects.
- Channels/enzymes/receptors targeted analgesia allows for a broader utilization of synergistic combinations of nonopioid analgesia and more refined and judicious use of opioids.
- The ideal path for safe and effective chronic pain management focuses on rigorous evaluation of the risk of opioids abuse, misuse, and safety, and on engagement and effective counseling on the risks and benefits of all analgesics.
and social disturbances, EPs have historically been encouraged to liberally use analgesics, in particular opioids, for pain, with the admonition that failure to do so will lead to subpar care and “oligoanalgesia.” Simultaneously, advocacy for attention to pain control with resultant increased and more widespread use of opioids in patients with both acute and chronic noncancer pain has led to significant public health and personal consequences of abuse, misuse, and diversion and their resultant morbidity and mortality.

Over the past 15 years significant advances have been made in our understanding of the neurobiological aspects of pain. These advances have led to a shift to mechanism-specific pain prevention and treatment approaches whenever possible. With this latter approach, the neurobiological abnormalities creating pain are identified and targeted with specific analgesics or interventions. This approach to the management of pain in the ED allows more refined and judicious use of opioid analgesics.

The purpose of this article is to review recent advances in the management of acute and chronic pain in the ED as well as to discuss several newer strategies and controversies.

**Acute Pain**

Acute pain management in the ED requires prompt recognition and assessment of a painful condition, timely initiation of safe and effective analgesia, and frequent reassessment and adjustment in therapy. In light of advances in the understanding of pain science, the pharmacologic armamentarium for ED analgesia has expanded dramatically over the past decade. It is recognized that most acute pain, like postoperative pain, tends to resolve rapidly over several days; most EPs prescribe for only a few days of outpatient analgesia. Similarly, there are concerns that when opioids are used too broadly for pain, the risk of long-term use, misuse, and abuse increases to unacceptable levels.

**Opioids**

Opioids are traditionally accepted as a cornerstone in acute pain management in the ED. Their effects occur primarily through μ-opioid receptor-mediated blockade of neurotransmitter release and pain transmission. The most commonly used opioids in the ED are pure μ-receptor agonists, such as morphine, hydromorphone, or hydrocodone. Because of highly variable interindividual dose-response relationships, for pure μ-opioid agonists, dosages should be titrated upward on a case-by-case basis until satisfactory pain relief is achieved or adverse effects become unacceptable.

Several controversies surround opioid administration in the ED for acute pain, including optimal opioid selection based on the indication (clinical circumstances and context), patient variables, pain severity, optimal dose and dosing regimen, and, in particular, appropriate prescribing practices on discharge.

**Parenteral (intravenous) dosing**

Proponents of weight-based dosing regimens advocate for morphine dosing of 0.1 mg/kg, hydromorphone of 0.015 mg/kg, or fentanyl of 1.5 mcg/kg. However, morphine given at 0.1 mg/kg as an initial dose demonstrates inadequate pain relief in a large proportion of patients with acute traumatic and nontraumatic pain. Studies demonstrated less than 50% reduction in pain score (less than 3 points on the numeric rating scale [NRS]) in 67% and 47% of patients at 30 minutes and 60 minutes, respectively; fentanyl rescue in 49% of patients with renal colic at 30 minutes; and lack of efficacy at 30 minutes compared with placebo in children with abdominal pain. Supporters of a fixed dosing regimen recommend administration of 4 mg of morphine or 1 mg of...
hydromorphone, as this regimen provided greater than 3 points change in pain score (NRS) regardless of patients’ weight.\textsuperscript{13–15} Unfortunately, fixed dosing regimens do not take into account the fact that different patients require different doses of opioids to treat similar painful conditions and that this variability in opioid dosing requirements cannot be reliably predicted. Therefore, the key to successful parenteral opioid analgesia is the titration of these analgesics. Morphine and hydromorphone titration protocols produced acceptable pain relief in 99% of and 96% of patients at 60 minutes.\textsuperscript{16,17}

**Nebulized/intranasal analgesia**

Nebulized and intranasal routes of opioid administration provide rapid and reliable noninvasive analgesia in the absence of exigent intravenous (IV) access. Fentanyl is considered safe and effective when administered via nebulization at doses of 3 to 4 µg/kg and intranasally at doses 1 to 2 µg/kg to adult and pediatric patients with acute abdominal pain and acute traumatic pain.\textsuperscript{18–20} One concern with the nebulized regimen is the potential variability in the dose actually administered, which may lead either to undertreatment of pain or to overdose. \textbf{Table 1} summarizes the dosing and titration intervals of commonly used opioids in the ED.

**Patient-controlled analgesia**

Patient-controlled analgesia (PCA) using morphine, hydromorphone, or fentanyl provides similar analgesic efficacy as does titrated IV analgesic and carries greater patient and nurses satisfaction.\textsuperscript{21,22} On the other hand, the use of PCA might result in oversedation and programming errors may lead to respiratory depression and greater time, effort, and expense.\textsuperscript{23} The overall incidence of respiratory depression in patients using PCA ranges from 0.1% to 0.8%, although higher rates of 1.1% to 3.9% have been found with concurrent basal infusion. From a risk-benefits perspective, elderly patients, patients with obstructive sleep apnea, and patients with concurrent sedatives and break-through opioid use are at greatest risk for respiratory depression and, therefore, should not be candidates for ED PCA.\textsuperscript{23}

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Routes</th>
<th>Dosing</th>
<th>Pitfalls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>IV: weight based</td>
<td>0.1–0.15 mg/kg</td>
<td>Titration at 20 min: if 10-mg dose use as a drip over 5–10 min</td>
</tr>
<tr>
<td></td>
<td>IV: fixed</td>
<td>2–4 mg</td>
<td>Titration at 10–15 min</td>
</tr>
<tr>
<td></td>
<td>SQ</td>
<td>2–4 mg</td>
<td>Titration at 10–15 min</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>2–4 mg</td>
<td>Unpredictable response/duration of analgesia</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>IV: weight based</td>
<td>0.015 mg/kg</td>
<td>Titration at 10–15 min</td>
</tr>
<tr>
<td></td>
<td>IV: fixed</td>
<td>0.25–1 mg</td>
<td>Titration at 10–15 min</td>
</tr>
<tr>
<td></td>
<td>IM</td>
<td>0.25–2 mg</td>
<td>Unpredictable response/duration of analgesia</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>IV: weight based</td>
<td>1.0–1.5 µg/kg</td>
<td>Titration at 10 min (if 100-µg dose, use a drip over 5–10 min)</td>
</tr>
<tr>
<td></td>
<td>IV: fixed</td>
<td>25–50 µg</td>
<td>Titration at 10 min</td>
</tr>
<tr>
<td></td>
<td>Nebulized</td>
<td>2–4 µg/kg</td>
<td>Use breath-actuated nebulizers (enclosed canister)</td>
</tr>
<tr>
<td></td>
<td>Intranasal</td>
<td>1–2 µg/kg</td>
<td>No more than 1 mL per nostril, titration at 10–15 min</td>
</tr>
</tbody>
</table>

\textit{Abbreviations:} IM, intramuscular; SQ, subcutaneous.
Nonsteroidal Antiinflammatory Drugs

Nonsteroidal antiinflammatory drugs (NSAIDs) have been used extensively for several decades for the management of a variety of acute and chronic painful conditions and remain among the most frequently used analgesics in the ED. They act primarily by inhibiting (reversibly) the activity of both cyclooxygenase (COX)-1 (constitutive) and COX-2 (inducible) enzymes and block the synthesis of prostaglandins and thromboxanes. NSAIDs are available in oral, rectal, topical (dermal cream), and parenteral formulations. From a clinical perspective, their utility in the ED is limited by an analgesic ceiling (ie, nontitratable dosing) and a potentially concerning side effect profile.

The analgesic ceiling refers to the dose of a drug beyond which any further dose increase will not result in additional analgesic efficacy. Thus, the analgesics ceiling for ibuprofen is 400 mg per dose (1200 mg/24 h) and for ketorolac is 10 mg per dose (10 mg/24 h). These doses are less than those often prescribed for control of inflammation and fever. When it comes to equipotent doses of different NSAIDs, there is no difference in analgesic efficacy. For example, there is similar analgesic efficacy between oral ibuprofen at 800 mg and intramuscular (IM) ketorolac at 60 mg. IV ketorolac is the most commonly administered parenteral NSAID in the ED; it is typically dosed at 30 mg IV and 60 mg IM, which is 3 to 6 times higher than its analgesic dose. In addition, IV ketorolac is useful in supplementing opioid and nonopioid analgesics in treating severe pain in the ED. Absolute contraindications to NSAIDs use in the ED include allergy to the specific NSAID or to another in the class, active peptic ulcer disease, and tenuous renal function. Relative contraindications include prior history of gastrointestinal hemorrhage, severe hypertension, hyperkalemia, hepatic insufficiency, bleeding disorder, prior myocardial infarctions (COX-2) or stroke (COX-1), congestive heart failure, recent major vascular and cardiac surgery, pregnant patients, and elderly patients. In the ED, the most common indications for the use of an NSAIDs are renal colic, headache for which bleeding is not a likely consideration, dental pain, and musculoskeletal pain and injury. These analgesics should be used at the lowest possible dose for the shortest period of time (no more than 5 days).

Acetaminophen

Acetaminophen (APAP) (paracetamol) is a p-aminophenol derivative with weak inhibitory activity of COX (COX-1, COX -2, and COX-3 isoenzymes) that translates into modest antiinflammatory and analgesic effects. APAP is available in oral, rectal, and IV formulation. Earlier data in surgical and anesthesia literature advocated heavily for use of IV APAP as a part of multimodal postoperative analgesia with an ability to reduce opioid consumption by 33% to 78%. Most recent trials of IV APAP, however, demonstrated a much lower opioid-sparing effect (18%–20%) and an inability to decrease opioid-induced nausea and vomiting (OINV).

Several randomized controlled trials in the ED evaluated analgesic efficacy and safety of IV APAP in treating patients with renal colic, traumatic musculoskeletal pain, and migraine headache. Out of 4 renal colic trials, the use of IV APAP demonstrated similar analgesic efficacy to 0.1 mg/kg morphine in 2 trials, although the other trials demonstrated less and greater pain relief than morphine, respectively. However, all trials showed significantly less side effects in the IV APAP group (primarily nausea and vomiting) in comparison with morphine. IV APAP had similar analgesic efficacy in controlling acute traumatic pain and acute migraine headache as morphine and NSAIDs with less side effects. The greatest limitation to the use of IV APAP is
the nearly 100-fold cost differential compared with oral formulations, which is likely not justified by any marginal improvement in pain relief. Perhaps when the price is lower, the cost-benefit relationship can be reassessed.

**Ketamine**

Ketamine is a noncompetitive N-methyl-D-aspartate (NMDA) and glutamate receptor antagonist that possesses analgesic, antihyperalgesic (opioid induced), and amnestic properties. Ketamine, at subdissociative doses (also known as low-dose ketamine or analgesic dose ketamine) of 0.1 to 0.4 mg/kg, provided effective analgesia as a single agent or as an adjunct to opioids (reducing the need for opioids) in the treatment of acute traumatic and nontraumatic pain in the ED. This effective analgesia, however, must be balanced against high rates of minor adverse side effects (14%–80%), though typically short-lived and not requiring intervention.

In addition, subdissociative dose ketamine (0.3 mg/kg IV) provided better pain relief at 5 to 15 minutes and comparable analgesic efficacy at 20 and 30 minutes in comparison with IV morphine (0.1 mg/kg) in patients with acute abdominal, flank, and back pain. However, there were higher rates of minor side effects at 5 and 15 minutes. Subsequent case series using short infusions of low-dose ketamine (0.3 mg/kg over 10 minutes) demonstrated significantly less side effects (6%) with effective analgesia (87%) compared with bolus dosing.

Furthermore, intranasal (IN) subdissociative dose ketamine administered at 1 mg/kg to children with acute traumatic limb injury demonstrates 60% decrease in pain scores at 30 minutes. Similarly, 1 mg/kg IN ketamine demonstrated similar analgesic efficacy when compared with IN fentanyl (1.5 mcg/kg) at 30 minutes, though with significantly higher rates of minor side effects. Lastly, IN ketamine at 0.5 to 0.75 mg/kg for patients with acute musculoskeletal trauma demonstrated significant pain relief in 88% of patients at 30 minutes with dizziness and feelings of unreality being the most frequent side effects (53% and 35%).

In summary, the use of IV subdissociative dose ketamine, either alone or in combination with opioids, is safe and effective for the treatment of acute pain and may be opioid sparing. Its use has been associated with relatively high rates of minor though short-lived adverse side effects that might be reduced by using a short infusion.

**Local Anesthetics**

Local anesthetics are widely used in the ED for topical, local, regional, intra-articular, and systemic anesthesia and analgesia. Local anesthetics (esters and amides) possess analgesic and antihyperalgesic properties by noncompetitively blocking neuronal sodium channels.

**Topical**

Topical analgesics containing lidocaine come in patches, ointments, and creams. These formulations have been used to treat pain from acute sprains, strains, and contusions as well as variety of acute inflammatory and chronic neuropathic conditions, including postherpetic neuralgia (PHN), complex regional pain syndromes (CRPS) and painful diabetic neuropathy (PDN). For example, a lidocaine patch 5% provided significant reduction of pain at rest and with movement in patients with acute herpes zoster infection with minimal side effects.

**Regional (ultrasound-guided nerve blocks)**

Ultrasound-guided regional anesthesia (UGRA) provides substantial pain relief, reduces systemic opioid requirements, results in high degrees of patient satisfaction,
and decreases resources utilization. It may replace procedural sedation for certain indications. Studies (case series and randomized trials) evaluating UGRA (eg, interscalene, supraclavicular, and forearm blocks) with either 1% lidocaine or 0.25% bupivacaine for patients with upper extremity trauma (fractures, dislocations) or infections (abscess) demonstrated complete pain control, total muscle relaxation, and successful completion of procedures. Similarly, studies describing UGRA for patients with lower extremity fractures or dislocations (eg, femoral nerve block, fascia iliaca compartment block) demonstrated significant pain control, decreased need for rescue analgesia, and first-attempt procedural success. In addition, UGRA demonstrated few procedural complications, minimal need for rescue analgesia, and great patient satisfaction.

**Intra-articular**

Intra-articular lidocaine (IAL) injection (with and without ultrasound guidance) for patients with acute shoulder dislocations has gained popularity among EPs. The available data demonstrate that IAL in the ED was associated with decreased length of stay (LOS), decreased overall cost of treatment, decreased complications rate, and modest effects on periprocedural pain relief and reduction success compared with standard reduction techniques.

**Systemic (intravenous)**

Analgesic efficacy and safety of IV lidocaine has been evaluated in patients with renal colic and acute lower back pain. IV lidocaine 2% without preservatives (ie, cardiac formulation) given at 1.5 mg/kg resulted in complete resolution of renal colic pain in 87% of patients in case series and significant pain decrease (greater than 3 on NRS) in 90% of subjects in randomized controlled trials. The most common (transient) side effects were dizziness and nausea. In addition, administration of 100 mg IV lidocaine improved the pain score in patients with acute lower back pain at 60 minutes but required rescue analgesia in 65% of patients. Although promising, this therapy will need to be studied in larger populations with underlying cardiac disease before it can be broadly used.

**Nitrous Oxide**

Nitrous oxide is a colorless, tasteless gas that provides analgesia by stabilizing the neurons in the brain to prevent action potential propagation and by interacting with the endogenous opioid system via a partial agonism at μ and κ opioid receptors. Nitrous oxide mixture (50:50) provided significant analgesia and reduction in anxiety to 1201 patients in a rural emergency services system, with 21% of patients developing minor side effects, mostly dizziness or lightheadedness. Nitrous oxide in combination with hematoma block was found to be more effective than ketamine/midazolam combination in relieving pain, to have shorter recovery times, and fewer adverse side effects for patients with forearm fracture. Nitrous oxide (50:50 mixture) demonstrated similar analgesic efficacy to IV fentanyl (2 μg/kg) and no difference in adverse effects in patients with long bone fracture.

**Channels/enzymes/receptors Targeted Analgesia Concept**

The channels/enzymes/receptors targeted analgesia (CERTA) concept is based on our improved understanding of the neurobiological aspect of pain with a shift from a symptom-based approach to pain to a mechanistic approach. This targeted analgesic approach allows for a broader utilization of synergistic combinations of nonopioid analgesia and more refined and judicious (rescue) use of opioids.
combinations result in greater analgesia, fewer side effects, lesser sedation, and shorter LOS. An example of this concept would include a combination of COX enzymes inhibitor (ketorolac) with a sodium channel-blocking agent (IV lidocaine) for patients with renal colic. Another example would include a combination of NMDA-receptor antagonist (ketamine) with sodium channel blockade (lidocaine via UGRA) for acute traumatic musculoskeletal pain. Table 2 summarizes possible combinations and their utilizations in the ED for pain management.

**CHRONIC PAIN**

Chronic noncancer pain is a multifactorial entity affecting social, behavioral, and psychological aspects of peoples’ lives and society in general. Chronic pain carries a significant societal burden that reportedly affects 31% of the adult population in the United States and costs between $560 and $635 billion annually, which is greater than the annual costs of heart disease ($309 billion), cancer ($243 billion), and diabetes ($188 billion).66

Unfortunately, as the use of opioid analgesics for treatment of chronic noncancer pain accelerated over the past 2 decades, significant increases in prescription opioid misuse, abuse, addiction, diversion, and opioid-related mortality have occurred. Between 1997 and 2007, the quantity of prescribed opioids increased by 866% overall and 380% for oxycodone and hydrocodone, respectively. Between 1997 and 2013, 175,000 deaths were reported due to prescription opioid overdose and the rates of addiction treatment from prescription opioid abuse increased by 900%.67

The rate of prescription opioid misuse (ie, not taking medication exactly as directed) among patients with chronic pain is as high as 24%, and rates of opioid use disorder are 26%.68,69 Opioids may also cause hyperalgesia (heightened pain perception to a noxious stimulus), especially when taken in high doses over prolonged periods of time-.69 Thus, the complexity of chronic pain requires a very comprehensive, multidisciplinary approach to its evaluation and management that includes identification and treatment of exacerbating factors, utilization of psychological treatment modalities, administration of nonopioid and adjuvant analgesics, treatment of associated behavioral disorders, and restoration of sleep and daily activities. Only after these measures are optimized should a trial of opioid therapy, or continuation of existing opioid therapy, be considered.70

The fast-paced environment of the ED, geared toward rapid treatment of acute injuries or illnesses, precludes EPs from investing significant amounts of time to communicate with patients with chronic pain, access past medical records, adequately assess patients’ risk for opioid abuse and misuse, or verify patient-physician agreements.70,71

However, EPs can use state prescription drug monitoring programs (PDMPs) where accessible to ensure patients’ safe opioid use by avoiding excessive dosing and drug interactions and by identifying aberrant use behaviors, or doctor shopping. In one study, implementation of such programs resulted in a change of the clinical management in 41% of cases, with most patients (61%) receiving less opioid analgesic than originally planned and 39% receiving more.72 Another trial demonstrated fair agreement between emergency provider impression of drug-seeking behavior and that suggested by the PDMP (κ = 0.30), with a resultant change in prescribing opioids at discharge in 9.5% of cases.73

The American College of Emergency Physicians and the American Academy of Emergency Medicine have created recommendations for EPs to assist in their analgesic practices for patients with chronic noncancer pain74,75 (Box 1). However, the
<table>
<thead>
<tr>
<th>Target Site</th>
<th>Medications/Dosing</th>
<th>Indications</th>
<th>Pain Syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium channels blockers</td>
<td><strong>Lidocaine:</strong></td>
<td>Chronic/acute MSK pain</td>
<td>Tendinitis, osteoarthritis, contusion</td>
</tr>
<tr>
<td></td>
<td>Topical: 5% Lidoderm patch</td>
<td></td>
<td>Traumatic injuries</td>
</tr>
<tr>
<td></td>
<td>Local: 1%–2% (4 mg/kg max)</td>
<td>Acute MSK pain</td>
<td>Traumatic injuries (fractures, dislocations)</td>
</tr>
<tr>
<td></td>
<td>Regional: 1%–2% (4 mg/kg max)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Intra-articular: 1% (20–30 mL)</td>
<td>Acute MSK pain</td>
<td>Dislocations (shoulder)</td>
</tr>
<tr>
<td></td>
<td>Systemic IV: 2% cardiac Lidocaine (1.5–2.0 mg/kg, max 200 mg)</td>
<td>Acute visceral pain</td>
<td>Renal colic</td>
</tr>
<tr>
<td></td>
<td><strong>Bupivacaine:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Local: 0.25%–0.5% (2.5 mg/kg max)</td>
<td>Acute MSK pain</td>
<td>Traumatic injuries (lacerations)</td>
</tr>
<tr>
<td></td>
<td>Regional: 0.25%–0.5% (2.5 mg/kg max)</td>
<td>Acute MSK pain</td>
<td>Traumatic injuries (fractures, dislocations)</td>
</tr>
<tr>
<td></td>
<td>Nortriptyline: 25 mg po</td>
<td>Chronic neuropathic pain</td>
<td>Postherpetic neuralgia, sciatica, diabetic neuropathy</td>
</tr>
<tr>
<td></td>
<td>Amitriptyline: 10 mg po</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium channels (central)</td>
<td>Gabapentin: 100–300 mg</td>
<td>Acute postoperative pain</td>
<td>Nerve palsy, neuralgias</td>
</tr>
<tr>
<td>blockers</td>
<td>Pregabalin: 25 mg po</td>
<td>Acute neuropathic pain</td>
<td>Diabetic neuropathy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Chronic neuropathic pain</td>
<td>Postherpetic Neuropathy, sciatica, fibromyalgia</td>
</tr>
<tr>
<td>Cox-1, -2, -3 enzymes</td>
<td><strong>NSAIDs:</strong></td>
<td>Acute MSK pain (trauma), headache,</td>
<td>Sprains, strains, contusions</td>
</tr>
<tr>
<td>inhibitors</td>
<td>Ibuprofen: 400 mg po</td>
<td>inflammatory pain chronic MSK pain</td>
<td>Chronic osteoarthritis, tendinopathies</td>
</tr>
<tr>
<td></td>
<td>Naproxen: 250–375–500 mg po</td>
<td>Acute MSK pain, acute abdominal pain</td>
<td>Renal colic, abdominal pain (nontraumatic), back pain, headache</td>
</tr>
<tr>
<td></td>
<td>Ketorolac IV: 10–30 mg</td>
<td></td>
<td>Sprains, strains, contusions</td>
</tr>
<tr>
<td></td>
<td>Topical:</td>
<td>Acute MSK pain</td>
<td>Chronic osteoarthritis, tendinopathies</td>
</tr>
<tr>
<td></td>
<td>Diclofenac 1% gel</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diclofenac 1.3% patch</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NMDA/glutamate receptors</td>
<td>Ketamine (subdissociative dosing):</td>
<td>Acute pain, opioid-tolerant pain, chronic pain</td>
<td>Traumatic pain, abdominal/flank/back pain, sickle cell pain, sciatica, abdominal migraine, neuropathic pain</td>
</tr>
<tr>
<td>antagonists</td>
<td>IV bolus: 0.1–0.4 mg/kg over 10 min</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV infusion: 0.15–0.25 mg/kg/h</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IN: 0.75–1.0 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SQ: 0.1–0.4 mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receptor Agonists</td>
<td>Drugs</td>
<td>Doses</td>
<td>Uses</td>
</tr>
<tr>
<td>------------------</td>
<td>-------</td>
<td>-------</td>
<td>------</td>
</tr>
<tr>
<td><strong>Central alpha 1, 2 receptors agonists</strong></td>
<td>Clonidine IV: 0.5–1.0 μg/kg</td>
<td>Acute pain, chronic pain</td>
<td>Adjunct to local anesthetics, opioids, ketamine for acute traumatic/nontraumatic pain</td>
</tr>
<tr>
<td></td>
<td>Dexmedetomidine IV: −0.5–1.0 μg/kg bolus, −0.1–0.5 μg/kg/h infusion</td>
<td>Acute pain, neuropathic pain, opioid-resistant pain</td>
<td>Sickle cell pain, CRPS, severe sciatica</td>
</tr>
<tr>
<td><strong>Opioid receptors agonists (μ-receptors)</strong></td>
<td>Morphine: (IV, SQ, remove) weight based, fixed</td>
<td>Acute traumatic/nontraumatic pain</td>
<td>Acute MSK pain (fractures), acute abdominal pain, acute traumatic/nontraumatic pain</td>
</tr>
<tr>
<td></td>
<td>Hydromorphone (IV, IM): weight based, fixed</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fentanyl (IV, IN, nebulization): weight based, fixed</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GABA receptors agonist</strong></td>
<td>Diprivan (propofol) IV: 10 mg q 5 min</td>
<td>Acute headache</td>
<td>Intractable migraine headache</td>
</tr>
<tr>
<td><strong>Volatile anesthetic (endogenous opioid receptors agonist)</strong></td>
<td>Nitrous oxide: 50/50 concentration</td>
<td>Acute pain: traumatic/nontraumatic</td>
<td>Fractures, dislocations, adjunct to local/regional blocks, opioids</td>
</tr>
<tr>
<td></td>
<td>70/30 concentration</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>D1-2 receptors antagonists</strong></td>
<td>Haladol IV: 1–2 mg</td>
<td>Acute pain</td>
<td>Migraine headache, chronic abdominal angina</td>
</tr>
<tr>
<td></td>
<td>Droperidol IV: 2–5 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metoclopramide IV: 10–20 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Promazine IV: 10 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5HT-2, 5HT-3 receptors antagonists</strong></td>
<td>Metoclopramide IV: 10–20 mg</td>
<td>Acute pain</td>
<td>Migraine headache</td>
</tr>
<tr>
<td></td>
<td>Haladol IV: 1–2 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Droperidol IV: 2–5 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>5HT-1 agonists</strong></td>
<td>Sumatriptan SQ: 4–6 mg</td>
<td>Acute pain</td>
<td>Migraine headache</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cluster headache</td>
</tr>
</tbody>
</table>
Box 1

Opioid-prescribing guidelines in treatment of chronic noncancer pain in the ED

1. The physician should honor existing patient-physician pain contracts and treatment agreements and consider past prescription patterns from information sources, such as centralized or state-specific PDMPs.

2. The physicians should avoid the routine prescribing of outpatient opioids for patients with acute exacerbation of chronic noncancer pain seen in the ED.

3. The physician should address acute exacerbation of chronic noncancer pain by using nonopioid analgesics, nonpharmacologic therapies, or referral to pain clinic/specialist for arranged follow-up if patients do not have a private physician.

4. If opioids are to prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration (3 days supply), and the physician should consider patients’ risk for opioid misuse, abuse, or diversion.

5. The physician should avoid initiating long-acting or extended-release opioids, such as oxycodone and methadone.

6. The physician should not replace lost, stolen, or destroyed prescription and should not refill chronic opioid prescriptions including ER/LA opioids.

7. The physician should avoid prescribing opioids to patients currently taking sedative-hypnotics medications or concurrent opioid analgesics.

8. The physician must provide information to patients regarding risks of using opioid analgesics, such as overdose, dependence, and addiction, as well as educate patients about safe storage and proper medication disposal.

9. The physician should offer an alternative to opioid analgesics to patients and should actively involve patients in their analgesic decision making.


The ED is a primary setting for medical care for many patients presenting with traumatic and nontraumatic painful conditions. In providing effective care to the populations served by the ED, EPs have a great responsibility to relieve pain by all possible appropriate means in a timely, efficient, and safe manner. The improvement in our understanding of the neurobiology of pain has lead to a great deal of utilization of nonopioid analgesia in the ED and, simultaneously, has led to more rational and safer opioid prescribing practices. We must promote patient-centered, pain-syndrome
targeted analgesia in the ED through education, collaboration, and exploration of more efficient and safer analgesics practices in the ED.

REFERENCES

17. Chang AK, Bijur PE, Campbell CM, et al. Safety and efficacy of rapid titration using 1mg doses of intravenous hydromorphone in emergency department


