26. ACUTE PAIN MANAGEMENT IN THE FIELD

INTRODUCTION

The management of pain in an austere environment depends on trained personnel who are motivated to aggressively treat acute pain. Efforts to improve perioperative pain management have centered on the development of acute pain service (APS) teams of healthcare professionals, usually directed by an anesthesiologist, who are organized and committed to the management of acute pain. The adoption of the APS model for effective pain management in austere environments by the US military is a logical approach. Without medical personnel tasked specifically with the APS function, pain treatment would revert to the low priority it has traditionally been given by surgeons and anesthesiologists. This is particularly true in the chaotic, high-stress, mass casualty medical environment of the battlefield or disaster scene.

Effective perioperative pain management depends on a multimodal approach to analgesia. Multimodal analgesia refers to the concept of using multiple analgesics and pain control technologies with different mechanisms of action. Not only will these components act synergistically to improve overall pain control, but this approach may also minimize the unwanted and possibly dangerous side effects of large doses of one medication. A significant advantage of multimodal analgesia in austere environments is the lower total dose needed for each drug component. Additionally, the multimodal analgesic approach offers a departure from the traditional opioid-only option in field medicine.

The following discussion and recommendations on commonly available pain medications is predicated on the existence of an APS. These guidelines are not intended to supersede medication package insert information or the physician's training in prescribing pain medication. The guidelines presented in this chapter are intended to serve as a starting point, but the physician must individualize acute pain care to each patient's needs and according to the environmental conditions.

OPIOIDS

Morphine remains the gold standard analgesic to which all other medications are compared. The ease of morphine administration following the invention of hollow hypodermic needles and syringes in the 1850s enhanced use and acceptance of the drug as an effective treatment for traumatic pain. The use of morphine for pain was widespread during the American Civil War (1861–1865) and Franco-Prussian War (1870–1871), but a lack of understanding of opioid use and side effects led to morphine addiction in many soldiers (known as "soldier's disease"). Despite the potential for life-threatening side effects, the success of opioids in treating pain in field medicine is beyond dispute. The challenge is to develop acute pain protocols and technologies that emphasize the beneficial pain relief properties of opioids while minimizing their side effects.

Casualty care advances in patients emerging from the conflicts in Iraq and Afghanistan have changed pain management attitudes and practices in the field environment. Although the lethality of weapons and severity of wounds continue to increase, casualty survival has never been higher. US military casualties from Iraq and Afghanistan currently have a 90% survival rate, compared to 76% during the Vietnam War, 67% during the Civil War, and 58% during the Revolutionary War. The increased survival rate results from many factors, including emphasis on early, advanced, far-forward surgical care; improved surgical and critical care techniques; availability of blood products; advances in body armor; and rapid ground and air evacuation to major medical facilities within and outside of the war zone. The rapid movement of casualties in particular has rendered opioid-based pain management protocols less appealing: the crowded, low-light, deafening, jolting, environment of evacuation aircraft makes monitoring difficult and magnifies the difficulties of opioid-only pain control therapy. Healthcare providers in this situation are less likely to use adequate doses of morphine because of valid patient safety concerns. The high numbers of healthcare providers in the evacuation chain and long evacuation distances further complicate opioid use. Many of these issues can be addressed by a multimodal pain therapy protocol, tailored to the austere medicine scenario, in which opioids are only part of the overall pain medication plan (Tables 26-1 and 26-2).

TABLE 26-1

SUGGESTED DOSAGES OF OPIOIDS FOR ACUTE PAIN CONTROL IN THE 70-KG OPIOID-NAIVE MILITARY CASUALTY

Opioid	Intravenous/ Intramuscular*	PCA†	Oral	Epidural‡	Intrathecal‡	Plasma Half-life	Comments§
Morphine	5–15 mg every 3–4 h	1–2 mg every 6–12 min	10–30 mg every 2–3 h	1–4 mg	100–300 μg	3 h (1–5 h)	Principal medical alkaloid of opium; causes active metabolites, respiratory depression, and increased intracranial pressure
Hydro-morphone	2–3 mg every 3–4 h	0.2–0.8 mg every 8–12 min	2–3 mg every 4–6 h	0.5–1 mg	100–200 μg	2–3 h	Semisynthetic opioid, approximately 5 times more potent than morphine and a useful alternative
Fentanyl	25–100 μg every 5 min titrated to effect at bedside	25–50 μg every 8–12 min, rare applications	Sublingual preparation available	50–100 μg	12.5–25 μg	7 h (3–12 h)	Synthetic; novel delivery technologies are in development
Meperidine	75–150 mg every 2–3 h	10 mg every 6–12 min, rare applications	100–300 mg every 3 h	NA	NA	3–5 h	Toxic metabolite normeperidine can lead to seizures; increased risk of abuse due to rapid onset and associated "rush"
Methadone	5–10 mg every 8–12 h short term use	NA	5–15 mg every 8–12 h short-term use	NA	NA	24–36 h	Synthetic; exhibits NMDA receptor antagonist activity; long half-life provides more stable analgesia compared to more frequently dosed opioids; usually reserved for level 4 use
Codeine	15–60 mg every 4 h IM only	NA	30–60 mg every 4 h	NA	NA	2–4 h	Antitussive; combined with acetaminophen as Tylenol-3¥; ineffective in 10% of Caucasians
Oxycodone	NA	NA	10–20 mg every 4–6 h	NA	NA	3–4.5 h	Combined with aspirin as Percodan¶ and acetaminophen as Percocet**; high abuse potential
Tramadol	50–100 mg every 4–6 h	NA	50–150 mg every 4–6 h	NA	NA	5–7 h	Respiratory depression is not a common side effect; can decrease the seizure threshold

*Generally, the intramuscular administration of opioids should be avoided in favor of intravenous administration.
†PCA is a preferred method for opioid pain control when equipment is available and the patient is able to operate the PCA device.
‡Epidural/intrathecal infusions of narcotics should be avoided in patients who may be transported to the next level of care within 24 hours.
§Naloxone is an opioid antagonist that reverses systemic opioid effects (analgesia, sedation, respiratory depression, etc) and should be available when opioids are used. Naloxone doses (0.2–0.04 mg) are titrated to desired effect every 2 to 3 minutes. The effect is dose dependent, lasting 20 to 60 minutes.
¥Johnson & Johnson, New Brunswick, NJ.
¶DuPont Pharmaceuticals, Wilmington, Del.
**Endo Pharmaceuticals, Chadds Ford, Pa.
IM: intramuscular
NA: not applicable
NMDA: *N*-methyl D-aspartate
PCA: patient-controlled analgesia

TABLE 26-2

EQUIANALGESIC OPIOID CONVERSION

Opioid	Intravenous (mg)	Oral (mg)	Epidural (mg)	Intrathecal (mg)
Morphine	1	3	0.1	0.01
Hydromorphone	0.2	0.6	0.02	0.002
Meperidine	10	3	NA	NA
Fentanyl	0.01	0.03	0.001	0.0001

NA: not applicable

N-METHYL D-ASPARTATE RECEPTOR ANTAGONISTS

Of the *N*-methyl D-aspartate (NMDA) antagonists, ketamine is the most commonly used and well-known example for use in austere conditions. It has been used extensively and exclusively for anesthesia in war casualties in a variety of conflicts and conditions. Ketamine's cardiovascular stimulating and bronchodilatory activity coupled with its profound amnestic and analgesic properties make it particularly useful in austere environments. For perioperative pain management, ketamine has been shown to provide an additive analgesic effect when used with other medications preemptively, in epidural catheters, and as an intravenous infusion following major surgery. Small-dose ketamine has been found to be a safe adjuvant to opioids when reduced narcotic use is desirable. A common concern among providers is ketamine's association with bad dreams, hallucinations, dizziness, dysphoria, disorientation, and confusion. However, recent evidence indicates no significant increase in central nervous system symptoms in patients receiving ketamine (via patient-controlled analgesia, intravenous infusion, continuous intravenous infusion, or epidural) compared to patients receiving opioids alone. Subanesthetic concentrations of ketamine can provide postoperative antihyperalgesia, analgesia, and an opioid-sparing effect when used in combination with opioid medications (Table 26-3).

TABLE 26-3

SUGGESTED DOSAGES OF KETAMINE FOR ACUTE PAIN CONTROL IN THE MILITARY CASUALTY*

Route	Dosage
Intravenous/Intramuscular	150–300 μg/kg loading dose
Continuous infusion	1–14 μg/kg/min
Oral	0.5 mg/kg
Epidural	30–60 mg
Intrathecal	NA

*The more active S-ketamine enantiomer is available. Ketamine is underutilized for acute pain control. Plasma half-life is 2.5 to 3 hours.
NA: not applicable

α_2-ANTAGONISTS

Clonidine and dexmedetomidine are α_2-adrenergic agonists that can produce a significant analgesic effect when used alone or in combination with other analgesics, without the respiratory depression associated with opioids. Clonidine's analgesic properties have been demonstrated whether the drug is administered intravenously, intrathecally, epidurally, intraarticularly, or as an adjunct to local anesthetics in a peripheral nerve block. The versatility of clonidine in providing anesthesia in a variety of clinical scenarios suggests it would be a useful addition to the field medicine medication list (Table 26-4). Dose-related side effects of clonidine include hypotension, bradycardia, and sedation. Dexmedetomidine, which is seven times more selective for α_2-adrenergic receptors though of shorter duration than clonidine, has also been used for perioperative pain management, although profound sedation can complicate its use. One important consideration when using these medications in austere conditions is their propensity to suppress thermoregulatory responses, thus promoting the development of hypothermia.

NONSTEROIDAL ANTIINFLAMMATORY DRUGS

Nonsteroidal antiinflammatory drugs (NSAIDs) are an important class of medications for austere environment analgesia when used as part of a multimodal pain management plan (Table 26-5). Acetaminophen (paracetamol) lacks some of the side effects associated with other NSAIDs, such as impaired platelet function, renal function, and bone growth. Although weak when used alone, acetaminophen enhances the analgesic effects of other NSAIDs and morphine when used concurrently. Oral NSAIDs block prostaglandin synthesis by inhibiting cyclooxygenase enzyme (COX) 1, thus reducing the inflammatory as well as the nociceptive response following injury (type 1 evidence). Newer (COX-2) NSAIDs lack the antiplatelet effects of the COX-1 NSAIDs, but have similar analgesic effects. Prolonged use of the COX-2 NSAIDs is controversial because of concerns over increased cardiovascular events. However, COX-2 NSAIDs decrease the possibility of respiratory depression and over-sedation, and for short-term use in a field setting, their advantages as adjunct analgesics for reducing opioid requirements far outweigh their disadvantages. Long shelf-life, ease of transport, and low abuse potential are additional benefits of NSAIDs in an austere environment. Some US military units have developed "wound packs" containing acetaminophen, a COX-2, and a fluoroquinolone, which the soldier is instructed to consume following a penetrating extremity wound. This approach is too new to determine its effectiveness, but the concept of prepackaged pain medications for use under defined conditions during war or disaster warrants further research and development. Parenteral preparations of NSAIDs, which further the potential utility of these medications in field medicine, are also available.

TABLE 26-4

SUGGESTED DOSAGES OF α_2-ADRENERGIC RECEPTOR AGONISTS FOR ACUTE PAIN MANAGEMENT IN THE MILITARY CASUALTY

α_2-Adrenergic Receptor Agonist	Intravenous/ Intramuscular	Continuous Infusion	Oral	Epidural	Intrathecal	Plasma Half-life	Comments
Clonidine*	2–5 μg/kg	0.3 μg/kg/h following loading bolus	2–5 μg/kg	3 μg/kg added to local anesthetic	15–30 μg added to local anesthetic	12–16 h	Hypotension, sedation, and bradycardia are important side effects; additive effect when used with opioids
Dexmedetomidine	1 μg/kg	0.4 μg/kg/h following loading bolus	NA	NA	NA	2 h	Pure α_2-adrenergic agonist; increases incidence of sedation and bradycardia

*Clonidine, 1 μg/kg, added to local anesthetic injected for peripheral nerve blocks prolongs block analgesia with minimal (sedation) to no side effects. NA: not applicable

TABLE 26-5

SUGGESTED DOSAGES OF NONSTEROIDAL ANTIINFLAMMATORY DRUGS FOR ACUTE PAIN MANAGEMENT IN THE MILITARY CASUALTY

NSAID	Intravenous/ Intramuscular	Oral	Plasma Half-life	Comments
Acetaminophen	NA	325–1,000 mg every 4–6 h up to 3,000 mg/day	1–4 h	Does not produce gastric irritation or alter platelet aggregation; weak antiinflammatory; hepatotoxic in large doses
Ketorolac	30 mg, then 15–30 mg every 6 h	10 mg every 4–6 h	5 h	30 mg intravenous is equivalent to 10 mg of morphine; moderate antiinflammatory activity; may cause life-threatening bronchospasm in asthma patients
Acetylsalicylic acid (aspirin)	NA	325–650 mg every 4–6 h	2–3 h	Antipyretic; low intensity pain; effective platelet activation inhibitor; useful for acute angina or myocardial infarction; can induce asthma in up to 20% of asthma patients
Ibuprofen	NA	400–800 mg every 8 h	2 h	Low incidence of gastrointestinal side effects
Naproxen	NA	250–500 mg every 12 h	12–15 h	Longer half-life allows twice daily dosing
Indomethacin	NA	25–50 mg every 8 h	4.5 h	Potent antiinflammatory
Celecoxib	NA	400 mg loading dose followed by 100–200 mg daily	11 h	Highly selective COX-2 inhibitor; greater cardiovascular risk than other NSAIDs

COX: cyclooxgenase
NA: not applicable
NSAID: nonsteroidal antiinflammatory drugs

ANTICONVULSANTS

Anticonvulsant medications such as gabapentin and pregabalin (in addition to the NMDA receptor antagonists already mentioned) are used in acute pain management as antihyperalgesic drugs to prevent the induction and maintenance of pain sensitization of the spinal cord dorsal horn and peripheral nerves following trauma (Table 26-6). In theory, preemptive analgesia, using a multimodal approach, can prevent or at least attenuate the unwanted neurophysiological and biochemical consequences of untreated pain. Gabapentin at a total dose of 3,000 mg in the first 24 hours following abdominal hysterectomy has been shown to significantly reduce morphine consumption with minimal side effects. Although definitive evidence is lacking, research has suggested that gabapentin use with other analgesic medications may protect the patient from central sensitization to pain following surgery. Gabapentin and pregabalin are currently used routinely in the pain management of US military casualties returning from Iraq and Afghanistan. Available evidence supports the inclusion of these medications in a field pain medicine plan.

TABLE 26-6

SUGGESTED DOSAGES OF ANTICONVULSANTS FOR ACUTE PAIN MANAGEMENT IN THE MILITARY CASUALTY

Anticonvulsant	Oral Dosage	Plasma Half-life	Comments
Gabapentin (Neurontin*)	100–300 mg every 8 h gradually increased as needed up to 3,600 mg daily in 3 divided doses	5–7 h	Therapeutic effect on neuropathic pain believed to be due to action on voltage-gated N-type calcium ion channels; somnolence and fatigue are side effects; does not appear to interact with other medications
Pregabalin (Lyrica*)	75 mg every 12 h increased as needed up to 300 mg in 2 divided doses	5–6 h	Similar to gabapentin but more potent; fewer dose-related side effects

*Pfizer Inc, New York, NY

TRICYCLIC ANTIDEPRESSANTS

Tricyclic antidepressants have been used to manage neuropathic pain for more than 20 years. Medications of this class act through the inhibition of norepinephrine and serotonin reuptake into postganglionic sympathetic nervous system nerve endings, enhancing the antinociceptive effects on these neurotransmitters. These medications are occasionally used following traumatic injury in combination with other pain medications as part of a multimodal approach. Early application of tricyclic antidepressants may have some benefit in preventing acute pain progression into chronic pain states (Table 26-7).

TABLE 26-7

SUGGESTED DOSAGES OF TRICYCLIC ANTIDEPRESSANTS FOR ACUTE PAIN MANAGEMENT IN THE MILITARY CASUALTY

Tricyclic Antidepressant	Oral	Plasma Half-life	Comments
Amitriptyline (Elavil*)	10–150 mg daily	12–24 h	Anticholinergic and sedative side effects; will enhance the response to other central nervous system depressants
Nortriptyline	25 mg every night up to a maximum of 150 mg every day	18–60 h	Fewer side effects; overactive or agitated patients may exhibit greater agitation

*Zeneca Pharmaceuticals, Wilmington, Del.

OTHER PAIN MEDICATIONS

Other nonopioid medications, such as adenosine, droperidol, magnesium, neostigmine, and opioid antagonists, have been successfully used in the management of postsurgical pain. However, the clinical advantages and disadvantages of these unconventional therapies will require further clarification before recommendations for use in an austere medical environment can be made. In addition to peripheral nerve blocks, local anesthetics can be very effective in the management of pain through subcutaneous injections around a wounded area or direct infusion into a wound using a catheter.

FUTURE PAIN CONTROL METHODS AND EQUIPMENT

Considerable effort to find methods other than intravenous morphine for pain management in battlefield scenarios has been made. Although the effectiveness of intravenous morphine is without question, the equipment and expertise to establish intravenous access may be lacking in austere battlefield or natural disaster situations. A possible alternative is transdermal delivery of fentanyl citrate, and a promising delivery device is the patient-controlled transdermal delivery system for fentanyl hydrochloride. The credit-card–sized device is placed on the patient's skin with adhesive and activated by the patient pushing a button. The device then delivers a 40-μg fentanyl dose over a 10-minute period through a process of iontophoresis (the introduction of medication into tissue through means on an electric current). Unlike transdermal fentanyl patches that continuously deliver medication passively and are inappropriate for opioid naive patients, the patient-controlled transdermal delivery system functions similar to a patient-controlled analgesia machine, and the two devices have been shown to be equally effective for perioperative pain control following major surgery. Oral transmucosal fentanyl is another delivery method with potential for use in austere environments. In 2003, 22 soldiers involved in the Iraq conflict were treated after mild injury with oral fentanyl lozenges (1,600 μg) in a field setting. The treatment was effective, although three soldiers complained of nausea and one required naloxone for hypoventilation, emphasizing that novel delivery systems for opioids do not eliminate the potential dangerous side effects of these drugs.

The administration of ketamine or hydromorphone intranasally using unit-dose nasal applicators has received substantial attention by the military for far-forward pain control following injury. Opioid use for pain can significantly degrade a soldier's ability to continue the mission because of its sedative effects. Theoretically, low-dose ketamine delivered intranasally reduces pain without substantially degrading performance. Although intranasal ketamine has been used successfully for breakthrough pain in chronic pain patients with minimal side effects, its abuse potential and possible cognitive effects in a high-stress environment warrants further study before recommendations on use in austere environments can be made. Intranasal delivery of hydromorphone does not change the side effects associated with opioids; however, this novel delivery system does not require intravenous access, which could be advantageous on the battlefield.

Finally, nonpharmacologic management of pain through proper splinting of fractures and protection of wounds from further jostling or impact is a vital consideration in any acute pain management plan. This is especially true during patient transport, when inadvertent impact or vibration can lead to extreme discomfort. The psychological benefits derived from healthcare provider attention to patient comfort during evacuation can greatly enhance the effectiveness of the multimodal pain care plan.