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Critical Care Pearls

- Pain continues to be undertreated in patients in intensive care units (ICUs).
- Untreated pain can lead to increased morbidity and mortality, decreased immunity, and increased length of stay.
- Opioids remain the principal drug group for pain management in the ICU.
- Other medications can and should be supplemented and tailored for the individual need to increase efficacy and reduce side effects.
- Local anesthetics, especially for neuraxial administration, are appropriate and recommended.

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Critically ill patients often fail to report accurately the extent and quality of the pain they experience and are thus likely to be undertreated. Their pain may arise from the disease process itself or as a consequence of diagnostic or therapeutic procedures. Between 55% and 75% of patients in an intensive care unit (ICU) with a present or past diagnosis of cancer report pain (1). Less than 20% of patients receive opiates before procedures (2).

The stress response to critical illness can have many deleterious effects. Unrelieved pain in critically ill patients can increase mortality, morbidity, length of stay, and use of resources (3). Appropriate use of sedation and analgesia can attenuate the stress response, alleviate pain and anxiety, and improve compliance with care (4). Three of the most common stressors among patients in the ICU are pain, sleep deprivation, and anxiety. Studies have shown each of these stressors is associated with decreased immune functioning (5).

Physiology of Pain

Pain may be somatic, visceral, or neuropathic. Somatic pain is caused by tissue injury; is well localized; and is sharp, aching, or gnawing in character. Visceral pain is caused by compression or distention and is vague, dull, or aching in character. It may be referred to other areas of the body. Neuropathic pain results from injury to the peripheral nerves or the central nervous system (6).

Free nerve endings (nociceptors) are stimulated by mechanical, thermal, or chemical stimuli. Three types of nerves convey the impulse forward. Large, thinly myelinated A delta fibers transmit intense mechanical stimuli. Unmyelinated C fibers respond to mechanical, thermal, and chemical stimuli.

Some A and C fibers respond to noxious mechanical and noxious heat stimuli. B fibers are myelinated preganglionic autonomic fibers.

Peripheral neurons project and synapse primarily in the dorsal horn of the spinal cord. From there, afferent neurons cross and ascend in the lateral spinothalmic tract to synapse in the thalamus. Perepheral transmission is modulated through substances such as bradykinins, serotonin, prostaglandins, and histamine. In the spinal cord, neurotransmitters such as acetylcholine, substance P, aspartate, and glutamate cause the modulation. From the brainstem, inhibitory tracts such as opioid pathways and alpha adrenergic pathways descend and synapse in the dorsal horn. They release inhibitory neurotransmitters, endorphins, and norepinephrine.

The cerebral cortex receives sensory input into the primary and secondary somatosensory areas, SI and SII. Cerebrovascular disease or injury in either the thalamus or cortex can produce a central neuropathic pain syndrome (7).

Pain Assessment

In critically ill patients, pain is assessed using various scales (Figure 20-1 and Table 20-1). The numeric scale measures pain from 0 to 10 with 0 being no pain and 10 for severe pain. The patient indicates the number which depicts the intensity of pain. The visual analogue scale is similar to numeric scales without the numbers. The Wong–Baker faces scale is mainly used for children but can be used for adult patients as well. The FLACC (face, legs, activity, cry, consolability) scale was also developed for use in children. The scores obtained from the FLACC scale are then evaluated using the 0-to-10 pain scale.

Available Classes of Drugs

The mainstay of treatment of patients in the ICU is opioids, but other classes of drugs can be and are used in conjunction with opioids. These include acetaminophen, nonsteroidal antiinflammatory drugs (NSAIDs), and cyclooxygenase-2 (COX-2) inhibitors, tricyclic antidepressants (TCAs) such as amitriptyline, and antineuropathic medications such as gabapentin.

An advantage of combining medications which act on different receptors or through different pathways is that the combination helps reduce the dose of each and decreases the incidence of side effects. This reduces the total dependence on opioids. In addition, local anesthetics can be used by various routes either as sole agents or as supplements to opioids and other medications.

Opioids

Most opioids are metabolized in the liver, and this depends on hepatic blood flow. Lipid-soluble agents have a fast clinical onset. Common side effects include nausea and vomiting due to stimulation of the chemoreceptor trigger zone, urinary retention, pruritis, biliary colic, decreased gastrointestinal tone and secretions, depression of respiration, and myocardial depression. Opioids initially decrease the respiratory rate, followed by decrease in the tidal volume. These respiratory effects are enhanced by other depressants and any existing pulmonary disease, both of which are common in patients in intensive care units (ICUs). Opioids also depress the cough reflex and response to the partial pressure of carbon dioxide. Rapid-acting and potent opioids can lead to skeletal muscle rigidity and difficulty in ventilating. Pertinent details about specific agents in this category follow.

Morphine Sulfate

Morphine has been the prototype to which other opioids and analgesics are compared. It acts on μ1 and μ2 receptors in the whole body and affects not only the central nervous system but other systems, including respiratory and gastrointestinal systems. Its analgesic effects depend on its action on brain, spinal cord, and other areas. It is hydrophilic and thus crosses the blood–brain barrier

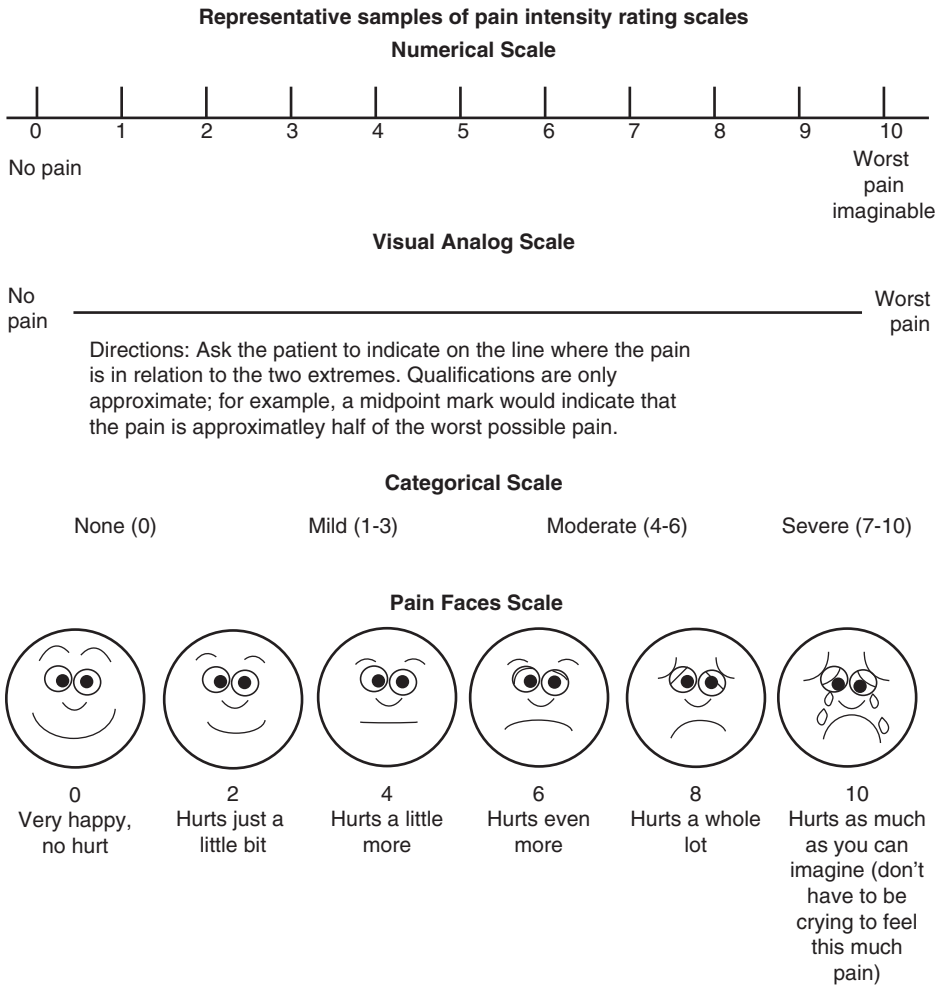

Figure 20-1 Representative samples of pain intensity rating scales. (The Wong-Baker FACES Pain Rating Scale. Adapted from Hockenberry MJ. Wong's Essentials of Pediatric Nursing, 7th edition. St. Louis: Mosby; 2005:1301; with permission.)

slowly. Peak blood levels occur approximately 20 minutes after administration. It is metabolized in the liver to morphine-6-glucuronide which also has analgesic effects. This metabolite is excreted by the kidneys and may accumulate in patients with renal failure.

Hydromorphone

Hydromorphone is a semisynthetic derivative of morphine which is ten times as potent as morphine. It has a relatively slow onset with a plasma half-life of two to three hours. A dose of 1.5 mg can be given every two to three hours (8).

Meperidine

Despite its higher incidence of side effects and accumulation of its metabolites, especially in renal disease, meperidine continues to be used extensively. It is available in Europe and Asia as pethidine. It is one-tenth as potent as morphine sulfate and acts

Table 20-1 FLACC Pain Scale

Categories	Scoring		
	0	**1**	**2**
Face	No particular expression or smile, eye contact and interest in surroundings	Occasional grimace or frown, withdrawn, disinterested, worried look to face, eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed	Frequent to constant frown, clenched jaw, quivering chin, deep furrows on forehead, eyes closed, mouth opened, deep lines around nose/lips
Legs	Normal position or relaxed	Uneasy, restless, tense, increased tone, rigidity, intermittent flexion/extension of limbs	Kicking or legs drawn up, hypertonicity, exaggerated flexion/extension of limbs, tremors
Activity	Lying quietly, normal position, moves easily and freely	Squirming, shifting back and forth, tense, hesitant to move, guarding, pressure on body part	Arched, rigid, or jerking, fixed position, rocking, side to side head movement, rubbing of body part
Cry	No cry/moan (awake or asleep)	Moans or whimpers, occasional cries, sighs, occasional complaint	Crying steadily, screams, sobs, moans, grunts, frequent complaints
Consolability	Calm, content, relaxed, does not require consoling	Reassured by occasional touching, hugging, or "talking to." Distractible	Difficult to console or comfort

Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from which results a total score between zero and ten.
The FLACC Pain Scale can be used with infant and pediatric patients aged 0-3 years, cognitively impaired patients, and those patients unable to use other scales. The words above that are **bold** apply to all patients EXCEPT infant and pediatric patients.
Assess the patient in each area – total the score – evaluate the total using the 0-10 pain scale parameters.
Adapted from Merkel SI, Voepal-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in children. Pediatric Nurse. 1997;23:293-7.

through the same receptors. It has a weak local anesthetic effect, and its analgesic effect correlates to its plasma concentration. Maximum plasma concentrations are achieved in 60 minutes. It is metabolized in the liver to normeperidine and meperidinic acid. The former can accumulate and cause central nervous system toxicity and seizures. Meperidine interacts with monoamine oxidase inhibitors leading to agitation, fever, and seizures. This progresses in some cases to apnea, coma, and death.

Fentanyl

Fentanyl is 50 to 100 times as potent as morphine; like meperidine, its analgesic effect relates to its plasma concentration. Fentanyl is very lipophilic and thus has a rapid onset but short duration of action secondary to redistribution. If large doses are given for prolonged periods of time, they saturate the redistribution sites and increase its duration of action. It is metabolized to norfentanyl. It can be given as a bolus or as continuous infusion at a rate of 50 to 100 µg/h. Transdermal fentanyl is available in doses of 25, 50, 75, and 100 µg. Table 20-2 provides a comparison of different opiates available.

Sufentanil

Sufentanil has a good safety profile and is five to ten times as potent as fentanyl. Peak levels

Table 20-2 Comparison of Common Opioids*

Drug	Oral (mg)	Parenteral (mg)
Morphine	30	10
Oxycodone	20	N/A
Hydromorphone	7.5	1.5
Fentanyl	N/A	0.1 (100 μg)
Codeine	200	30
Hydrocodone	20	N/A

*Doses referenced are selected solely for the purposes of comparison.

are achieved in three to five minutes, and effects last from half hour to one hour. Continuous infusion for analgesia is suitable for short-stay intensive care patients. For patients with longer stays, this can be supplemented with midazolam and clonidine (9).

Mixed Agonists and Antagonists

These include buprenorphine, butorphanol, dezocine, nalbuphine, and pentazocine. Depending on the agent chosen, they may be given intravenously (IV), intramuscularly, and, in case of pentazocine, orally. They may reverse agonist effects of opioids and lead to withdrawal symptoms.

Tramadol

Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine. It acts centrally by acting on μ receptors and inhibition of norepinephrine and serotonin reuptake. It is one- tenth as potent as morphine and has fewer respiratory effects. It is given for moderate pain.

Local Anesthetics

Local anesthetics can be used for pain relief, but these are underutilized. These can be used for infiltration into the tissues, nerve blocks, and neuraxial administration. A continuous infusion of bupivacaine is effective for decreasing pain and the need for opioid analgesics as well as improving patient satisfaction with their management after cardiac surgery. Patients are able to ambulate earlier, leading to reduced length of hospital stay.

These anesthetics are weak bases with charged and uncharged forms. There are two classes of local anesthetics: amides like lidocaine, mepivacaine, etidocaine, ropivacaine, and bupivacaine and esters like procaine, cocaine, chloroprocaine, and tetracaine. The first class is metabolized in liver, and the latter is hydrolyzed by ester hydrolysis.

Local anesthetics block nerve conduction by impairing the action potential in axons and inhibiting sodium influx. Increased lipid solubility increases the potency and increased protein binding increases their duration of action. The speed of onset of action is measured by pK_a, which is the pH at which they are 50% charged. Increased dose prolongs the action of the block.

True allergic reactions to local anesthetics are rare; ester local anesthetics may cause this through the metabolite p-aminobenzoic acid. Local anesthetics can also cause systemic toxicity. This results from an inadvertent intravascular injection or administration of a large dose. Central nervous system effects of toxicity include light-headedness, tinnitus, metallic taste, and numbness of mouth and lips; toxicity may lead to seizures and coma. Cardiovascular effects include decreased ventricular contractility leading to cardiovascular collapse. This necessitates oxygen therapy, medications, cardioversion, and even prolonged cardiopulmonary resuscitation.

Acetaminophen

This analgesic is commonly used and can be combined with other drugs like NSAIDs. The maximum daily dose is 4 g in adults and 90 mg/kg in children. The toxic dose may be lower with patients with alcoholism and with other susceptible individuals. When recommended doses are followed, the risk of hepatotoxicity is extremely small.

Aspirin, NSAIDs, and COX-2 Inhibitors

Aspirin was discovered in the eighteenth century. It has been used for many years as an

antiinflammatory, analgesic, and recently as an antiplatelet drug.

NSAIDs act by inhibiting the COX enzyme, which leads to the inhibition of prostaglandin synthesis. It has been suggested that inhibition of COX-2 may be related to the therapeutic effects of NSAIDs, and inhibition of COX-1 may lead to their adverse effects. These include commonly used drugs like ibuprofen, naproxyn, and diclofenac and are potent medications used extensively in pain management. They act peripherally at the pain site. Ketoralic is an NSAID available for intramuscular or IV administration and is often used in the postoperative period. Common side effects include gastrointestinal bleeding, fluid retention, renal damage, and decreased platelet aggregation.

COX-2 selective inhibitors are relatively recent antiinflammatory drugs. They are confirmed to have less gastrointestinal toxicity than nonselective, nonaspirin NSAIDs (4,10,11). However, these trials have raised concerns about the cardiovascular risks of this class of drugs (12). They fell in disrepute after withdrawal of rofecoxib (Bextra, Pfizer) and valdecoxib (Vioxx, Merck), following reports of excessive cardiac morbidity. Currently only celecoxib (Celebrex, Pfizer) is available for use.

Other Classes

N-methyl-D-aspartate (NMDA) antagonists such as ketamine and α2-adrenoceptor agonists such as clonidine are reasonable additions to other pain medications. Ketamine produces a dissociative state with amnesia and profound analgesia. Clonidine acts centrally and is used primarily as an antihypertensive. It has antinociceptive properties leading to its use in pain relief; it is often administered in conjunction with local anesthetics and opioids. It stimulates α2-receptors in the depressor area of the vasomotor center, leading to decreased outflow of sympathetic nervous system impulses to the periphery (13).

Modes of Delivery

The oral route is the most common route of delivery of all medications including analgesics. This access may be limited or not available in patients in the ICU. Advantages of this route include safety, simplicity, ease of administration, and economy. Disadvantages include slow onset, difficulty of titration, and the necessity of an intact absorption system.

Parenteral routes can be used; IV is preferred because intramuscular absorption is sometimes unreliable. Advantages of IV administration include quick onset and ease of titration. Medications can be administered as boluses or as continuous infusion. Patient-controlled administration systems are available, in which a bolus dose can be combined with a basal infusion.

Neuraxial administration such as epidural and spinal routes is commonly used and is appropriate for postoperative patients, trauma patients, cancer patients, and others. Opioids and local anesthetics are safe and effective. The number of drugs that can be used by this route have considerably increased in last few years. By interrupting pain pathways at the level of the first- and second-order neurons, a method of providing effective analgesia without the associated central nervous system depression and cyclical nature of pain associated with other parentral routes is achieved (14). Continuous local infusion of local anesthetics is effective for pain relief and shortens time to recovery. However, it is not widely employed. In one study of infusion at the median sternotomy site, patients in the bupivacaine group were able to ambulate earlier, leading to a reduced length of hospital stay (15).

Summary

Pain management in the ICU requires careful selection of medications and routes of administration. In this setting, patients are more

vulnerable than the general population to adverse effects and higher doses. Using more than one drug from different classes may work synergistically, keeping the dosage of each low and avoiding these adverse effects. Knowledge of the pharmacology of various medications and physiological status of patients is essential.

REFERENCES

1. **Nelson JE, Meier DE, Oei EJ, et al.** Self reported experience of critically ill patients receiving intensive care. Crit Care Med. 2001;29:277-82.
2. **Puntillo KA, White C, Morris AB, et al.** Patients' perceptions and responses to procedural pain: results from Thunder Project II. Am J Crit Care. 2001;10:238-51.
3. **Cheever KH.** Reducing the effects of acute pain in critically ill patients. Dimens Crit Care Nurs. 1999;18:14-23.
4. **Silverstein FE, Faich G, Goldstein JL, et al.** Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. JAMA. 2000;284:1247-55.
5. **DeKeyser F.** Psychoneuroimmunology in critically ill patients. AACN Clin Issues 2003; 14:25-32.
6. **Hurford EH, Bailin MT, Davison JK, et al.** Clinical anesthesia procedures of Massachusetts General Hospital. Philadelphia: Lippincot-Raven; 1997:661-88.
7. **Ashburn MA, Rice LJ.** The Management of Pain. New York: Churchill Livingstone; 1968:11.
8. **Borsook D, McPeek B.** The Massachusetts General Hospital Handbook of Pain Management. Boston: Little, Brown; 1996:68.
9. **Wappler F, Scolz J, Prause A, et al.** Level concept of analgesic dosing in intensive care medicine with sufentanil. Anesthesiol Intensivmed Notfallmed Schmerzther. 1998; 33:8-26.
10. **Bombardier C, Laine L, Reicin A, et al.** Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. N Engl J Med. 2000;343:1520-8.
11. **Schnitzer TJ, Burmester GR, Mysler E, et al.** Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), reduction in ulcer complications: randomised controlled trial. Lancet. 2004; 364:665-74.
12. **Mukherjee D, Nissen SE, Topol EJ.** Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA. 2001;286:954-9.
13. **Stoelting RK, Miller RD.** Basics of Anesthesia. New York: Churchill Livingstone; 1994:33-45.
14. **Barash PG, Cullen FC, Stoelting RK.** Handbook of Clinical Anesthesia. New York: Lippincot-Raven; 1997:1305-37.
15. **White PF, Rawal S, Latham P, et al.** Use of continuous local anesthetic infusion for pain management after median sternotomy. Anesthesiology. 2003;99:918-23.