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Continuing Education

Perioperative Pain Management Strategies in the Age of an Opioid Epidemic

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A B S T R A C T

According to the US Department of Health and Human Services 2016 and 2017 data, an estimated 130 people per day died from opioid-related drug overdoses; 42,249 people died from overdosing on opioids; and 2.1 million people had opioid-use disorder. Health care organizations such as the American Association of Nurse Anesthetists, the Association of periOperative Registered Nurses, the American Society of PeriAnesthesia Nurses, the American Society of Anesthesiologists, the American College of Surgeons, and the American Medical Association have information related to pain management and/or the opioid epidemic on their Web sites. It is imperative for health care providers to be cognizant of, and use low-dose opioid/opioid-free pain management therapies. This article reviews the pain process and outlines low-dose opioid/opioid-free pain management modalities.

Objectives—1. Examine strategies to mitigate the opioid crisis. 2. Describe multimodal approaches to analgesia. 3. Discuss locations in the pain pathway on which adjuvant drug classes work to reduce pain. 4. Identify the primary goals for an ERAS protocol.

The numbers are staggering. According to the US Department of Health and Human Services (HHS) 2016 and 2017 data, an estimated 130 people per day died from opioid-related drug overdoses; 42,249 people died from overdosing on opioids; and 2.1 million people had opioid-use disorder.[1] The opioid epidemic is so extreme that in 2017, HHS declared it a public health emergency.[1] In October 2018, President Trump signed the bipartisan bill *The Support for Patients and Communities Act*. Some highlights of this bill are increasing access to opioid addiction treatment; making it more difficult for synthetic opioids to cross the border; expanding a program to encourage more first responders to carry naloxone (opioid reversal); encouraging research on addiction and pain; increasing penalties related to overprescribing opioids; and raising awareness about appropriate pain treatment.[2] Several governmental agencies are responding to the opioid epidemic. HHS has five major priorities related to the opioid epidemic: access to treatment/recovery services, use of opioid reversal drugs, better surveillance of opioid use, pain/addiction research, and pain management advances.[3] The National Institutes of Health launched the Helping to End Addiction Long-term initiative in April 2018. This initiative focuses on research to improve treatments for opioid misuse and addiction and enhance pain management.[4] The Health Resources and Services Administration supports several initiatives such as expanding access through health centers and other primary care settings, using telehealth to treat opioid-use disorder, connecting stakeholders to opioid-related resources, sharing best practices and approaches, increasing opioid-use disorder training in primary care, informing policy and future investments, and addressing opioid-related poisonings and overdoses.[5]

Health care organizations such as the American Association of Nurse Anesthetists, the Association of periOperative Registered Nurses, the American Society of PeriAnesthesia Nurses, the American Society of Anesthesiologists, the American College of Surgeons, and the American Medical Association have information related to pain management and/or the opioid epidemic on their Web sites. The American Association of Nurse Anesthetists has an entire section of its Web site dedicated to opioid crisis resources.[6] The resources include tools for patients and health care providers to make meaningful decisions related to acute and

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chronic pain management, opioid safety, substance use disorder, and others.

What can we, as health care providers, do to help mitigate this epidemic? We can use alternative nonopioid (or low-opioid) strategies to treat perioperative patient pain. Several strategies for perioperative pain control will be discussed in this article, including enhanced recovery after surgery (ERAS), regional anesthesia techniques, multimodal pharmacologic techniques, and nonpharmacologic techniques; but first, an overview of pain will be discussed.

Physiology of Pain

According to the International Association for the Study of Pain, pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage and is always subjective.[7] Pain is subjective and may be a physiological, an emotional, and/or a behavioral experience.[7,8] Acute pain is distinguished from chronic pain by the length of time it is experienced. Typically, acute pain lasts for less than 6 months and is caused by injury, disease process, or abnormal function of muscles or viscera.[9(pp1,047),10] Unrelieved acute pain can turn into chronic pain.

Pain can be classified based on pathophysiology (ie, nociceptive, nonnociceptive). Nociceptive pain is divided into somatic and visceral pain. Somatic pain is sharp, localized, and can result from damage to skin, tissues, bones, or joints.[8,11] Visceral pain can be described as dull, cramping, referred, and is associated with hollow organ or smooth muscle pain.[8,11] Nociceptive pain may be caused by mechanical (ie, trauma), thermal (ie, burn), or chemical (ie, poison) injuries.[10] Non-nociceptive pain is divided into neuropathic pain and inflammatory pain. Neuropathic pain is often characterized by numbness, tingling, burning, hyperalgesia, or allodynia (pain from a stimulus that normally does not cause pain).[8,11] Inflammatory pain results from mediators released at the site of tissue inflammation.[8,11] These mediators sensitize the nociceptive pain pathway.[11] Other types of pain include cancer pain, headache/migraine pain, and generalized pain (fibromyalgia).

Pain is processed through signal transduction, transmission, perception, and modulation.[8,10] Transduction is the process by which nociceptors (free nerve endings) detect a noxious stimulus (chemical, mechanical, and thermal) and transforms that stimulus into an action potential.[8,10] A-delta primary afferent fibers transmit fast, sharp, localized pain, which in turn, evokes withdrawal from the mechanical or thermal mechanism.[8,11] For example, if I am walking on the beach and step on a sea urchin, the noxious stimulus (sea urchin sharp spine) turns into an action potential, causing me to lift my foot off the sea urchin. C primary afferent fibers transmit slow dull, burning, throbbing, and aching pain. Peripheral tissue damage causes the release of chemical mediators and neurotransmitters from nociceptors. The most common chemical mediators and neurotransmitters are found in Table 1.

Analgesic therapies that target transduction include nonsteroidal anti-inflammatory drugs (NSAIDs), antihistamines, membrane-stabilizing agents (ie, gabapentin, pregabalin), local anesthetic topical agents, opioids, bradykinin, and serotonin antagonists.[12] Transmission is the process by which nerve impulses travel from the periphery to the central nervous system. As stated previously, A-delta fibers transmit fast sharp pain, and C fibers transmit slow chronic pain. The nerve impulses travel to the dorsal horn of the spinal cord and are further transmitted to the brain via neurons that cross the spinal cord. Analgesic therapies that target transmission include the use of local anesthetics in peripheral nerve blocks, plexus blocks, and epidural blocks.[12] Perception occurs when the pain impulse reaches the brain and is recognized as pain by a conscious person. Analgesic therapies targeting perception include parenteral opioids, alpha-2 agonists (ie, clonidine, tizanidine, dexmedetomidine), and general anesthesia.[12] Modulation is not well understood, but it inhibits or enhances pain signals via descending efferent pathways. Modulation is thought to inhibit pain via the release of neurotransmitters. Fear and anxiety can enhance modulation of pain signals. Analgesia therapies targeting modulation include spinal opioids, alpha-2 agonists, *N*-methyl-D-aspartate (NMDA) receptor antagonists (ie, ketamine, methadone), cholecystokinin antagonists, nitric oxide inhibitors, and potassium channel openers.[12]

Enhanced Recovery After Surgery

ERAS protocols have been around for 2 decades, although groundwork for a multimodal approach for early rehabilitation began in the 1990s.[13] The multimodal perioperative care perspective is focused on actions and measures to reduce surgical stress, improve hemodynamic function, and reduce time to mobilization postoperatively.[14] Authors agree that implementing ERAS protocols can reduce length of stay and morbidity, as well as speed recovery times.[15] Originally developed to reduce complications after colon surgery, early researchers realized that optimization of the patient by fluid management and alterations in fasting parameters preoperatively played a large role in the outcomes.[16-18] Aasa et al[19] recognized that developing a trusting relationship and gathering abundant information preoperatively can potentially build the foundation for personalized care while engaging the patient in the self-care necessary after the surgical procedure.

The ERAS protocol begins in the preoperative period and ends with discharge and patient education for continued home wellness. One of the mistakes made in intensive care medicine is the neglect of recovery measures.[15,20] This neglect can impact success and derail measures taken to promote ERAS before intensive care unit admission. In 2010, the ERAS Society was formed as a nonprofit organization to develop and provide guidance and support to others desiring evidence-based multimodal techniques to promote healing and decrease complications after surgery.[21-23] As of 2018, there were multiple societies and groups continuing to research

Table 1
Common Chemical Mediators and Neurotransmitters Related to Pain

Chemical Mediator or Neurotransmitter	Description
Substance P	Amino acid peptide excitatory neurotransmitter that facilitates pain transmission via activation of neurokinin-1 receptor. Released from peripheral afferent C fibers
Glutamate	Predominant excitatory neurotransmitter. Located in brain, spine, and periphery. Produces initial, fast, and sharp pain
Bradykinin	Peptide released amid inflammation process
Histamine	Released from mast cell granules, basophils, and platelets; substance P induces release of histamine
Serotonin	Released from platelets after tissue injury
Prostaglandins	Act as mediators of inflammation and sensitize peripheral nociceptors
Cytokines	Released in response to inflammation process; can lead to increased prostaglandin production
Calcitonin gene-related peptide	Released from peripheral afferent C fibers

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Table 2
Preoperative and Postoperative Considerations

Issue	Preoperative	Postoperative
Nausea	Ondansetron IV dosing Preoperative IV fluids Altering fasting requirements	Ondansetron, promethazine avoid narcotics Early oral nutrition
Pain	Dosing with NSAIDs Regional anesthesia blocks	NSAIDs Regional anesthesia blocks Local infiltration Gabapentin/anticonvulsant
Stress	Anxiolytics	Pain control/reduction Anxiolytics
Ileus	Altered fasting requirements Isovolemia	Isovolemia Early ambulation

IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs.

and develop ERAS protocols and guidelines, including anesthesia organizations.

With regards to ERAS analgesic management, analgesia using nonopioid and low-dose opioid techniques has been demonstrated to be adequate using a multimodal approach.[24,25] Various pharmacologic agents have been investigated separately and in combination as part of the multimodal model to control pain.[14,24-26]

Pain control during the postoperative period may be accomplished using a multimodal approach. Celecoxib, acetaminophen, ketorolac, gabapentin, and small-dose ketamine in combination reduced the number of opioids prescribed during the postoperative period.[27,28] Xu et al[29] also found a decrease in opioid administration, length of stay, and ileus formation using a multimodal approach. Ileus formation may be reduced using a nonopioid multimodal approach to postoperative pain control because it may allow earlier ambulation.

ERAS analgesic management based on a multimodal approach is addressed in the ERAS Society guidelines.[30] Management of pain using both anesthetic technique selection and nonopioid postoperative pain management are considerations that may be used to improve analgesia. Use of both systemic and regional anesthetic techniques is a focus of the ERAS Society guidelines. Additional foci include reduced neural and hormonal stress responses to surgery, early oral nutrition, and early mobilization to reduce postoperative complications and improve pain management.[30] Pharmacologic and nonpharmacologic techniques are also included in the ERAS guidelines and include intravenous (IV) adjuvants as well as local infiltration with local anesthetics as methods for pain control.[31] Table 2 includes preoperative and postoperative considerations.

Regional Anesthesia

Adequate postoperative pain management is very important. Poorly controlled postoperative pain is the primary reason for unanticipated postoperative admissions and readmissions.[12] Undertreated acute postoperative pain increases risk of progressing to chronic pain. In addition, it may delay mobilization and ambulation, which may lead to increased risk of deep vein thrombosis, insomnia, and depression. Local anesthetics block signal transduction of pain, and when combined with peripheral nerve blocks, prevents pain transmission.[12]

Regional block technique is commonly used as a perioperative and postoperative pain control measure. The history of regional blocks began in 1894 with the specificity theory by Von Frey, which linked specific nerve endings in skin to the sensation of pain.[32] Regional blocks cover most surgical procedures and are used to manage extended postoperative pain control to minimize narcotic usages.[33,34]

The development of newer and safer local anesthetic drugs, needles, and techniques has expanded use of neural blocks for the enhancement of surgery and pain management. Today, nerve stimulators and ultrasound imaging enhance regional blocks to simplify, refine, and increase safety of perioperative and postoperative pain management.[33,35] The great benefit of this advancement is a decreased reliance on narcotic agents.

Table 3
Regional Blocks and Their Indications

Type	Specific Blocks	Indications
Central (neuraxial block)	Spinal	Vaginal delivery, cesarean section Anorectal, genital, pelvic procedure Lower extremity, hernia, intra-abdominal surgery
	Epidural	Labor, vaginal delivery, perineum procedure Thoracotomy, gastric and colon resection, prostatectomy, hysterectomy, aortic aneurysm repair
	Caudal	Perineum, hernia procedure on pediatric population
Peripheral blocks	Cervical plexus block	Carotid endarterectomy, superficial neck procedure
Upper extremity blocks	Interscalene block	Shoulder, arm, forearm
	Supraclavicular/infraclavicular block	Arm, elbow, forearm, wrist, hand procedure
	Axillary brachial plexus block	Forearm, wrist, hand procedure
	IV (bier block)	Ganglion cyst, carpal tunnel release, tendon release
	Wrist block	Hands, fingers
	Digital block	Fingers
Truncal blocks	Transverse abdominal plane blocks	Bowel resections, ventral hernia repair, cholecystectomy Kidney transplant, total abdominal hysterectomy, C-section
	Paravertebral block	Mastectomy
	Intercostal nerve block	Chest-tube insertion
Lower extremity blocks	Lumbar plexus (psoas compartment block)	Lower limb procedure, tourniquet pain management Knee, thigh, hip, and femur fracture, stump pain
	Femoral nerve block	Femur, total knee arthroplasty, medial ankle
	Popliteal sciatic nerve block	Postoperative knee, calf, foot, ankle foot
	Saphenous nerve block	Vein harvest or stripping, medial foot, ankle
	Ankle block	Diabetic ulcers, gangrenous toes, bunions and bone spurs
Other blocks	Retrobulbar/peribulbar block	Intraocular lens implantation, posterior chamber/retinal surgery, corneal transplant, cataract surgery
	Airway block	Suspected difficult intubation, upper airway trauma, cervical spine fractures or radiculopathy, airway malignancy or abscess

IV, intravenous.

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Table 4
Nonopioid Pharmacologic Agents and Their Pain Pathway Interference

Drug Classification	Examples	Pain Pathway Interference
NSAIDs	Acetaminophen, ketorolac	Signal transmission: interferes with prostaglandin release
Gabapentenoids	Gabapentin, pregabalin	Signal transmission: inhibits neurotransmitter release by inhibiting presynaptic CA^{++} release; uses alpha-2 receptors
NMDA receptor antagonists	Ketamine, dextromethorphan, memantine, magnesium	Receptor level: inactivates NMDA receptor
Alpha-2 adrenergic agonists	Clonidine, dexmedetomidine	Signal transmission: inhibits neurotransmitter release centrally and peripherally; uses G protein–coupled alpha-2 receptors
Glucocorticoids	Dexamethasone	Signal transmission: interferes with prostaglandin release
Selective COX-2 inhibitors	Celecoxib, etoricoxib	Signal transmission: interferes with prostaglandin release
Local anesthetics	Lidocaine	Action potential: interferes with propagation of action potential through NA^{++} channel blockade
Other	Antidepressants: calcitonin, nicotine, capsaicin, cannabinoid	Exact mechanisms largely unknown; subject of research

NSAIDs, nonsteroidal anti-inflammatory drugs; CA^{++}, calcium ions; NMDA, *N*-methyl-D-aspartate; COX-2, cyclooxygenase-2; NA^{++}, sodium ions.

Table 3 illustrates regional anesthetic techniques and their indications.

Multimodal Pharmacologic Approach

Analgesia using nonopioid and low-dose opioid techniques in ERAS patients has been demonstrated to be adequate using a multimodal approach.[24,25] The intent of multimodal intervention is to minimize acute perioperative pain, while at the same time decreasing opioid requirements and associated adverse effects.[36-38] This synergistic and additive approach targets pain pathways at differing anatomic and pain receptor sites.[37] Coupled with postoperative acute pain treatment, multimodal preoperative and perioperative pharmacologic interventions combine to offer a comprehensive approach to pain prevention and treatment.[28,36-41]

Various pharmacologic agents have been investigated separately and in combination as part of the multimodal model to control pain.[24,25,37] Used aside from or in conjunction with opioids, common primary nonopioid pain treatments include NSAIDS, ketorolac, and acetaminophen. Although these agents have differing mechanisms of action, they all target disruption of prostaglandin synthesis. Although not directly responsible for producing pain, prostaglandins represent a vital step in the pain pathway, acting both centrally and peripherally.[12] The demand of nonopioid pain treatments has yielded ongoing research and development of IV preparations for faster onset in the postoperative care unit. As an example, acetaminophen IV, when given perioperatively, has been shown to decrease the occurrence of pain in the postanesthesia care unit.[28]

Adjuvant pharmacologic classes include gabapentenoids, NMDA receptor antagonists, alpha-2 adrenergic agonists, glucocorticoids, selective cyclooxygenase-2 (COX-2) inhibitors, and many others.[12,28,36-47] Equally important to improved pain control, studies show that many of these agents correlate with decreased opioid-induced side effects and postanesthesia care unit lengths of stay.[39-41] Where in the pain pathway do these adjuvant classes work? Gabapentenoids, traditionally used as antiepileptic agents, work presynaptically (alpha-2) to inhibit calcium release, which in turn prevents excitatory neurotransmitter release.[42] NMDA receptor antagonists work at the receptor level to prevent activation of the NMDA receptor.[12] Alpha-2 adrenergic agonists work both centrally and peripherally. G protein–coupled alpha-2 receptors at both presynaptic and postsynaptic sites are targeted, resulting in reducing neurotransmitter release. Glucocorticoids inhibit prostaglandin release by preventing the formation of arachidonic acid, a needed element in the inflammatory and pain pathway.[12] Selective COX-2 inhibitors inhibit prostaglandin release in a mechanism similar to NSAIDs and ketorolac. However, celecoxib and etoricoxib are more highly selective, resulting in a reduced number of side effects.[45] Differing from the other adjuvants, local anesthetics work to stop the propagation of the action potential through sodium channel blockade, resulting in a blockade of pain.[14] Finally, other adjuvant agents used for analgesia include antidepressants, calcitonin, nicotine, capsaicin, and cannabis. These agents are common topics of evidence-based research, as exact mechanisms of action, risk-benefit strategies, and efficacies are examined.[44-47] Table 4 illustrates nonopioid pharmacologic agents and their pain pathway interference.

Nonpharmacologic Approaches for Pain Relief

Various nonpharmacologic pain therapies exist; however, there is not enough evidence to make strong recommendations for which therapy should be used for postoperative pain relief. Some of these therapies include massage, acupuncture/acupressure, cold therapy, transcutaneous electrical nerve stimulation, cognitive behavioral modalities, and music therapy.[48,49] Cognitive behavioral modalities may include hypnosis, guided imagery, relaxation techniques, and intraoperative suggestions while under anesthesia.[48] Only the use of transcutaneous electrical nerve stimulation and cognitive behavioral modalities has been recommended as nonpharmacologic therapeutic modalities in conjunction with multimodal analgesic techniques for treatment of postoperative pain.[48]

Box 1
Selected Opioid Crisis Resources

Organization	Web Site
AANA	https://www.aana.com/practice/clinical-practice-resources/opioid-crisis-resources
ANA	https://www.nursingworld.org/practice-policy/work-environment/health-safety/opioid-epidemic/
ASA	https://www.asahq.org/in-the-spotlight/opioid-crisis
ERAS	http://erassociety.org/
Society for Opioid Free Anesthesia	https://goopioidfree.com/
HRSA	https://www.hrsa.gov/opioids
NIH	https://www.nih.gov/news-events/opioids-digital-press-kit

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Conclusion

As health care providers, we are responsible for ensuring the safety of our patients throughout the perioperative period. This includes using nonopioid and opioid-sparing techniques to manage patient pain. ERAS, regional anesthesia techniques, multimodal pharmacologic techniques, and nonpharmacologic pain relief techniques should be used in the perioperative period. Interprofessional communication and collaboration are vital to ensure safe evidence-based pain management. Resources related to the opioid crisis and management of patients with opioid use disorder are found in Box 1.

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Test ID W030920 – Expiration Date March 31, 2022

Perioperative Pain Management Strategies in the Age of an Opioid Crisis

1.5 Contact Hours
Purpose of the Journal of PeriAnesthesia Nursing: To facilitate communication about and deliver education specific to the body of knowledge unique to the practice of perianesthesia nursing.

Outcome of this CNE Activity: To enable the nurse to increase knowledge on perioperative pain management

Target Audience: All perianesthesia nurses

Article Objectives
1. Describe strategies to mitigate the opioid crisis.
2. Describe multimodal approaches to analgesia.
3. Discuss locations in the pain pathway on which adjuvant drug classes work to reduce pain.
4. Identify the primary goals for an Early Recovery After Surgery (ERAS) Protocol.

Accreditation
American Society of Perianesthesia Nurses is accredited with distinction as a provider of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.

Provider approved by the California Board of Registered Nursing, Provider Number CEP5197, for 1.5 contact hours.

Additional provider numbers: Alabama #ABNP0074

Contact hours: Registered nurse participants can receive 1.5 contact hours for this activity.

Disclosure
All planners and authors of continuing nursing education activities are required to disclose any significant financial relationships with the manufacturer(s) of any commercial products, goods or services. Any conflicts of interest must be resolved prior to the development of the educational activity. Such disclosures are included below.

Planners and Author Disclosures
The members of the planning committee for this continuing nursing education activity do not have any financial arrangements, interests or affiliations related to the subject matter of this continuing education activity to disclose.

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Requirements for Successful Completion: To receive contact hours for this continuing nursing education activity you must complete the registration form and payment, read the article, complete the online posttest and achieve a minimum grade of 100%, and complete the online evaluation.

Directions
A multiple-choice examination, designed to test your understanding of **Perioperative Pain Management Strategies in the Age of an Opioid Crisis** according to the objectives listed, is available on the ASPAN website: https://learn.aspan.org/

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