

Principles of Burn Pain Management

Dominika Lipowska James, MD*, Maryam Jowza, MD

KEYWORDS

- Pain burn pathophysiology • Adjuvant pain medications • Alternative pain therapy
- Opioid-based analgesia • Opioid tolerance • Opioid-induced hyperalgesia • Multimodal analgesia
- Patient-controlled analgesia

KEY POINTS

- Successfully managed acute pain improves trauma-related morbidity and mortality, and is associated with decreased likelihood of development of psychiatric comorbidities and chronic pain conditions.
- Proper pain assessment and monitoring, including frequent treatment plan and dose adjustments, is of primary importance.
- Opioid requirements of burn patients, in particular those with prior history of opioid use, substantially exceed average dosing recommendations. Identification of opioid-tolerant burn patients early in course of treatment improves analgesic outcomes.
- Opioids remain the cornerstone of acute pain treatment but should not be used as monotherapy.
- Multimodal pain management, including adjuvant pain medications, interventional blocks, alternative therapies, psychological counseling, physical and occupational therapy, results in optimal treatment outcomes and should be continued long term, even after the time of discharge.

Managing pain in a patient with burn injury can be complex. Pain that originates with burn injury is generally classified temporally, first as the pain in the acute process, then as the pain in the chronic phase when the bulk of tissue healing has occurred.

THE MECHANISM OF PAIN IN BURNS

The skin contains nociceptors that respond to heat and mechanical and chemical stimulation. Thermoreceptors interpret temperatures above 42°C as painful. Mechanoreceptors respond to changes caused by physical interactions, such as pressure of vibration. Chemical nociceptors are activated by endogenous chemicals, such as those released during an inflammatory process (ie, histamine, leukotrienes, and substance P), or exogenous

chemicals, such as contact with caustic or acidic materials.

In the immediate postburn injury period, tissue injury causes release of inflammatory mediators. These mediators sensitize the nociceptors at the area of injury. Pain transmission is facilitated by C-fibers, which are unmyelinated, and A-delta fibers, which are thinly myelinated. These signals are transmitted to the dorsal horn of the spinal cord. The clinical result is that the site of the injury is sensitized to all stimuli.¹ Clinically, this is experienced as increase sensitivity to touch, such as with wound care and topical agent administration in the area that is injured. This is called primary hyperalgesia.

Soon afterward, the area surrounding the area of tissue injury also becomes sensitized. This is called secondary hyperalgesia. This is thought to

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Department of Anesthesiology, University of North Carolina, Chapel Hill, NC, USA

* Corresponding author. Department of Anesthesiology, University of North Carolina, N2198 UNC Hospitals, CB # 7010, Chapel Hill, NC 27599-7010.

E-mail address: djames@aims.unc.edu

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be mediated by the spinal cord and due to sensitization of a larger nociceptive field from continuous afferent firing by nearby nociceptors.

DEPTH OF TISSUE INJURY AND PAIN

Burn severity is classified by the extent of involvement in body surface area affected and depth of skin injury. In first-degree burns, tissue injury is superficial and involves only the epidermis. Pain associated with this is generally mild to moderate and healing occurs within a week.²

Second-degree burns involve parts of the dermis. These are thought to be painful because there is damage to skin nociceptors and exposure of nerve endings. With healing, nerve regeneration can be disordered, leading to neuropathic pain.

Third-degree burns involve destruction of nociceptors and can make the affected area insensate. It would seem then, that these injuries should not be painful. However, in reality, deep burns contain areas of more shallow burn where nerve endings have not been completely destroyed; thus even full-thickness burns are painful.³

CATEGORIES OF BURN PAIN

There are 2 categories of pain experienced in burn injury.

Evoked and procedural pain occurs with predictable events, such as after a procedure, or with activities such as movement, physical therapy (PT), or dressing changes. This is generally short-lived but high in intensity.

Background pain is experienced without provocation and is present even at rest. Generally, it is thought to be less intense than evoked pain but, in contradistinction, it is constant. It can have spontaneous exacerbations with no known reason.

Inpatient Pain Management

The acute phase of burn pain management generally takes place in an inpatient setting. In a burn patient, the experience of pain is that of a chronic baseline pain negatively accentuated by frequent procedures such as surgeries, dressing changes, and procedures. Periprocedural pain often escalates, requiring an individualized treatment plan involving continuous monitoring, reassessment, and analgesic dose adjustments. In addition to this constant nociceptive input, the anticipation of pain leads to psychological trauma, which further intensifies the pain perception. Perioperative and periprocedural pain management is important because adequate pain management decreases morbidity and mortality, as well as the

likelihood of development of persistent postoperative pain. Inadequate pain control is also associated with a wide range of psychiatric conditions, including post-traumatic stress disorder (PTSD), depression, anxiety, and sleep disorders. Effective analgesia facilitates patient participation in rehabilitation and recovery.

OPIOIDS

Opioids remain the mainstay of treatment, especially in the acute phase of burn pain, and are the most efficacious medication in perioperative moderate and severe pain management. Opioids come in a variety of routes of delivery (by mouth, intravenous [IV], transdermal, sublingual, rectal) and formulations (short-acting, long-acting), which allows for flexibility of administration. Opioids are thought not to have a ceiling effect, thus they can be escalated to a therapeutic effect unless side effects preclude further dose escalation. Unlike other analgesics, opioids do not lead to renal or hepatic dysfunction, though choice of agent and dosing should include consideration of the patient's comorbidities.

Opioids, however, can cause a multitude of side effects that are often related to dose. These can range from simply bothersome effects, such as constipation, nausea, and itching, to severe effects, such as respiratory depression leading to death. Respiratory side effects may be especially pronounced in patients with pre-existing conditions such as sleep apnea, pulmonary comorbidities, and obesity. The incidence of side effects in patients managed for acute pain with opioids is high, with some studies finding that up to 92% of patients experience at least 1 side effect and 76% of patients experience 2 or more side effects.⁴

Despite increased risk of side effects, significant opioid dose escalation may be required for burn patients with extended hospital stays, patients requiring frequent procedures, or those with a history of prior opioid use or abuse. To optimize analgesic outcomes and decrease the likelihood of opioid-related side effects, patients should undergo frequent pain reassessments with judicious dose escalation, which are particularly important during the acute phase of injury and in the immediate postoperative period. Opioid-related side effects are less likely to occur with frequent small dose changes as opposed to infrequent large dose changes.

Tolerance and Opioid-Induced Hyperalgesia

With prolonged opioid use, changes in the central nervous system occur, leading to a decrease in

analgesic responsiveness to opioids.⁵⁻⁷ This process is referred to as tolerance. Tolerance can occur during the hospitalization period and in some patients as rapidly as within the perioperative period. Studies suggest that tolerance can occur even with an intraoperative infusion of a short-acting opioid.⁸ Tolerance is well known to occur in patients on chronic opioid therapy; however, it can also occur in opioid-naïve patients who are acutely exposed to opioids. Tolerance partially explains the need for dose escalation. Although tolerance to the analgesic effects of opioids occurs, tolerance to certain side effects, such as constipation or itching, does not develop.

Tolerance can be confused with opioid-induced hyperalgesia (OIH),⁵⁻⁷ which is defined as intensification of pain in the context of opioid use. In OIH, nociceptors become sensitized as a result of exposure to opioids. Patients can experience increased pain from painful and nonpainful stimuli (hyperalgesia and allodynia, respectively). OIH may occur irrespective of duration of opioid exposure or opioid dose. There is growing evidence that ultrashort-acting opioids, such as remifentanyl, may induce this phenomenon and perhaps should be avoided in burn injury patients.^{9,10} Opioid dose reduction can be helpful in improving analgesia but is a difficult therapy for patients to accept.

Clinically, both tolerance and OIH manifest as an intensification of the patient's pain experience, suggesting a need for opioid dose escalation. This can further be confused with pseudoaddiction, which appears as opioid-seeking behavior but is a result of inadequate pain control rather than addiction.

Ultimately, it is important to recognize that burn patients' opioid requirements, especially for patients who were previously on opioid therapy, substantially exceed standard dosing recommendations. Identification of patients with a history of long-term opioid use early in course of treatment ensures proper opioid dosing and better analgesic success. Although identification of opioid tolerance in trauma patients may be challenging due to inability to communicate, the patient's family, primary care provider, and review of controlled substance database and toxicology screen can be helpful.¹¹

Patient-Controlled Analgesia

The most common route of opioid administration in the immediate postburn injury period is IV. Opioids may be administered either as nurse-administered boluses, or via a patient-controlled analgesia (PCA) device. For severely critically ill

patients, the route of delivery is generally through a continuous IV infusion because patients are often incapacitated and unconscious. Continuous opioid infusions are appropriate in patients who are in an intensive care unit setting where the risk of opioid-related respiratory depression is continuously monitored. This form of administration should be used with great caution in unmonitored settings.

One of the most common methods of IV opioid administration to burn patients is via a PCA. This form of delivery has the benefit of flexible administration, circumventing delays associated with nursing care, and overall contributing to improved patient satisfaction. When dosed appropriately, PCA is immediate, safe, and efficacious, leading to a sense of control and empowerment thus decreasing anxiety. PCA analgesia can be particularly valuable during dressing changes and PT.^{12,13} Similar to other opioid formulations, effectiveness of PCA depends not only on proper PCA prescription (bolus dose, frequency of administration, and lockout interval) but, perhaps more importantly, on regular monitoring of patient's analgesic response and frequent dose adjustments. When determining proper opioid dosing, one should consider that chronic opioid users are thought to require, on average, 3 to 4 times more daily morphine milliequivalents than opioid-naïve patients.¹⁴

Opioids administered via PCA are thought to be less likely associated with risk of inadvertent respiratory depression or overdose; however, PCA use is not void of complications. Most PCA-related incidents are secondary to inappropriate PCA technique understanding by the patient, opioid dose administration by individuals other than the patient, or erroneous PCA prescription or programming. In addition, most PCA overdose incidents occur among patients receiving concurrent baseline opioid infusion and/or treatment with other sedatives (ie, benzodiazepines).

In most cases, baseline infusions are not recommended because they are associated with increased risk of side effects and overall escalation in opioid use, with no notable improvement in analgesia.¹⁵ Exceptions may apply to some opioid-tolerant patients with high daily opioid requirements who often need substantial and rapid PCA opioid dose escalation, which predisposes them to the sedative effects, in particular when combined with other respiratory depressants, such as benzodiazepines.

To achieve optimal analgesic efficacy and safety, PCA opioid administration should be individualized. Consideration should be given to the patient's age, weight, health status, opioid tolerance, extent of injuries, and coexisting comorbidities (eg, history

of apnea, respiratory conditions, renal or hepatic impairment). The PCA should be viewed as a method of delivering analgesia for breakthrough pain. Additional time-released opioid medications should be concurrently provided to achieve continuous therapeutic serum opioid levels, without the need for unremitting PCA use. This approach allows for PCA-free time, such as during rest or sleep. Initiation of PCA must be preceded by an opioid bolus in an effort to quickly achieve therapeutic serum levels required for adequate analgesia. Repeat boluses may be further required after prolonged periods of decreased PCA use (on awakening) or at a time of increased analgesic need (eg, dressing changes, PT).

Treatment of Patients on Buprenorphine Therapy

Buprenorphine is used to treat opioid addiction. It is available in a sublingual form as Subutex and, to deter from misuse, it is also available in a formulation with naloxone as Suboxone. It is a partial mu agonist, with strong affinity to the mu-opioid receptor. As a result, it only partially activates the mu-receptor and also makes it more difficult for other mu agonists (opioids) to fully activate the receptor. In patients on buprenorphine therapy, the analgesic effect of other opioids is attenuated.

This poses a problem for a patient who is on Suboxone or Subutex and unexpectedly presents with an acute injury. In such a situation, the authors' recommendation is to continue buprenorphine therapy only if the degree of injury is mild and recovery is expected to be quick and not particularly painful. It is imperative to recognize that patients who are maintained on buprenorphine will require much higher doses of a full opioid agonist to obtain analgesia.¹⁶

If the injury or the healing process is anticipated to be prolonged and painful, it is best to discontinue buprenorphine therapy and treat with a full opioid agonist for pain.

Another alternative is to use buprenorphine as an analgesic. This is best for situations in which pain associated with the injury is mild to moderate because, as mentioned previously, buprenorphine is a partial agonist and, as a result, there is a ceiling effect to the analgesic properties. Buprenorphine maintains an analgesic effect for 6 to 8 hours, so appropriate dosing for pain is every 6 to 8 hours as opposed to the once-daily dosing used for maintenance.

Methadone

Methadone has both opioid and nonopioid actions. Nonopioid actions include inhibition of the

reuptake of monoamines (eg, serotonin, norepinephrine) and inhibition of *N*-methyl-D-aspartate (NMDA) receptor, pharmacologic actions that result in additional analgesia. Activation of the NMDA receptor can produce central sensitization (ie, lowering central nervous system pain thresholds); blocking this receptor may help mitigate the development of hyperalgesia and tolerance. NMDA receptor antagonism may also be helpful in treatment of neuropathic pain states.^{17,18} Methadone has gained popularity as an analgesic for this purpose. It can be particularly helpful as an analgesic for burn patients who have developed tolerance and/or hyperalgesia as a result of prolonged opioid exposure.

It should be cautioned that methadone possesses idiosyncrasies that can make its use by inexperienced prescribers dangerous. Methadone is unique in that it has a variable terminal half-life that ranges between 7 and 65 hours. In other words, it will not reach steady state for several days after initiation or dosage adjustments. Too rapid or aggressive dose escalations can lead to drug accumulation and respiratory depression. Fortunately, renal and hepatic dysfunction is not known to cause methadone accumulation.^{19,20}

Methadone also has the ability to prolong the QT interval. Though the dose at which this is most likely to occur is still not agreed on, it is well accepted that this is an unlikely occurrence at doses below 100 mg per day.²¹ QT prolongation, however, can be more common in critically ill patients who may also necessitate life-saving medications known to prolong the QT interval, such as antimicrobials and antiarrhythmics, in the setting of frequent electrolyte disturbances.

Continuous methadone infusions and enteral methadone have been described to provide analgesia in critically injured burn patients and to help with weaning high-dose opioids and facilitate discontinuation of mechanical ventilation.²²

OPIOID-SPARING TECHNIQUES

Multimodal analgesia is an effective method for pain control that is based on the theory of targeting pain from multiple sites of action. The rationale behind this approach is that analgesics act synergistically and when used in combination can provide improved effectiveness at lower doses than can a single agent. Because side effects are frequently tied to dose, with more side effects at higher doses, a multimodal regimen also decreases potential for side effects.²³

The next section reviews 5 agents commonly used as part of a multimodal regimen.

Acetaminophen

Acetaminophen is a well-known analgesic with a mechanism of action that has yet to be defined. Studies suggest that there may be involvement of multiple receptor types, including cannabinoid receptors, and also inhibition of prostaglandin synthesis.²⁴ Clinical studies in surgical patients show improvement in pain and lowered opioid consumption with acetaminophen use. There is a ceiling effect with respect to analgesia and acetaminophen by itself is rarely appropriate for the treatment of burn pain in an acute inpatient setting. It is best used in combination with other adjuncts.

Nonsteroidal Anti-inflammatory Drugs

Like acetaminophen, nonsteroidal anti-inflammatory drugs are widely used analgesics. They are potent anti-inflammatory medications with mechanism of action that this is generally thought to be through inhibition of the enzymes that synthesize prostaglandin. However, a variety of other peripheral and central mechanisms are also emerging that is beyond the scope of this article. Their utilization for patients with acute burn injury is limited by side effects such as gastric ulceration and renal insufficiency. Their use can reduce the amount of opioid needed by up to 20% to 30% because these drugs act synergistically with opioids.²⁵

Antidepressants

Antidepressant medications are gaining recognition for their role as part of a multimodal treatment in chronic pain. The class of antidepressants most recognized for their analgesic properties in neuropathic chronic pain states are the tricyclic antidepressants (TCAs) and the combined serotonin and norepinephrine reuptake inhibitors (SNRIs). Of the TCAs, amitriptyline and nortriptyline are agents more frequently used for pain. The SNRIs include duloxetine, milnacipran, and venlafaxine. Like the SNRIs, the TCAs block reuptake of serotonin and norepinephrine.

The analgesic effect of antidepressants does not correlate with the treatment of depression. In fact, for the TCAs the analgesic benefit occurs before the anticipated effect on mood (about 2 weeks for pain vs 6–8 weeks for mood). It should be stressed that antidepressants cannot be used for acute control of pain because their dose may need to be titrated and adjusted slowly to minimize side effects. Further, the doses used for analgesia are typically lower than those used for the treatment of a mood disorder and serum levels do not correlate with degree of analgesia.

The analgesic action of these medications is thought to occur at the level of the spinal cord through bulbospinal pathway, which is a descending inhibitory pathway that modulates dorsal horn function. By blocking uptake of serotonin and norepinephrine, TCAs and SNRIs increase the activity of descending inhibitory pathways. There is probably also a supraspinal pathway mode of action, but this has yet to be determined.

These medications have not formally been studied in pain related to burn injury. Their use in burns is extrapolated from experience with treating chronic pain disorders. With respect to pain disorders, antidepressants are most widely used to neuropathic pain, such as with peripheral neuropathy, and centralized pain states, such as in fibromyalgia. Because acute burn pain often becomes long-lasting and can remain severe, it can take on neuropathic features with elements of central sensitization. Furthermore, neuropathy is commonly also seen in later stages of burn injury as dysesthesias and itching. Antidepressants can also be used for their opioid-sparing effect.

Common side effects of TCAs are largely due to antimuscarinic and antihistaminic effects. These include dry mouth, urinary retention, constipation, and sedation. SNRIs, which are newer than TCAs, are thought to have fewer associated side effects.

Antiepileptics

Antiepileptic medications are increasingly used to treat neuropathic pain states. In burn injury, in which there is a widespread damage to cutaneous nociceptors, many patients experience pain that is described as pins and needles, or itching, in addition to burning. These pain descriptors are hallmarks of neuropathic pain states. Furthermore, with a large injury and pain that is present for a substantial length of time, there is potential for central sensitization, further making the case that burn injury has a neuropathic component.

The gabapentinoids, pregabalin, and gabapentin have been studied in burn patients. Gabapentin has been shown to reduce pain scores, decrease opioid consumption, and decrease the burning pain.^{26,27} Similarly, pregabalin has been shown to be helpful in reducing the unpleasantness of pain, as well as procedural pain.²⁸

Other antiepileptics used in pain management include topiramate, oxcarbazepine, and carbamazepine. However, there are few data on their use in burn injury. Side effects of these medications include electrolyte disturbance with topiramate and oxcarbazepine, and aplastic anemia and Stevens-Johnson syndrome with carbamazepine.

Ketamine

Ketamine is a potent analgesic that is an NMDA receptor antagonist. Its hallmark property is the ability to produce a dissociative state when used at anesthetic doses (see later discussion).

NONPHARMACOLOGIC APPROACHES

Nonpharmacologic therapies have been studied in burn patients. There is a growing body of research in support of hypnosis for acute pain control in burns.²⁹ With this modality, patients are prepped by a hypnotist before painful stimuli, such as wound care or debridements, and are given post-hypnotic suggestions that aim to reduce pain and anxiety. Results so far have been promising.

Another modality that has utility in burn patients is cognitive behavioral therapy. In cognitive behavioral therapy, therapists work with patients to reframe thoughts about pain. A common teaching to patients is that although some sensations may hurt, they will not cause harm.

Virtual reality is a tool that has been studied predominantly in burn patients undergoing burn care and rehabilitation. Results from the studies show that patients who are immersed in a virtual reality report decreased associate pain and anxiety.³⁰

The most simple and cost-effective nonpharmacological aspect of care, however, is minimizing aspects of care that generate pain and timing interventions appropriately. In the example of dressing changes, pain can be ameliorated with moistening adherent dressings and avoiding drafts because exposure of wounds to the air can be a source of pain. Furthermore, adjusting air and water temperatures during hydrotherapy, and premedicating patients effectively before such interventions, will also reduce discomfort.³¹

Intraoperative or Perioperative Pain Management

Stress response to burn injury, as well as to surgical and procedural interventions that follow, can be associated with significant morbidity and mortality. Proper perioperative and perioperative pain control is of paramount importance. Inadequately treated pain has been associated with elevated levels of stress cytokines and catecholamines, as well as cortisol and adrenocorticotropic hormone elevation, resulting in activation of renin-angiotensin system, ultimately contributing to unfavorable medical outcomes. Optimal perioperative pain management should continue preoperative multimodal pain therapy. Intraoperative analgesic efforts should focus on aggressive opioid therapy in conjunction with nonopioid

agents such as ketamine, lidocaine, dexmedetomidine, and, if not contraindicated, Toradol. When appropriate, regional anesthesia should be considered.

OPIOIDS

Perioperative opioid requirements in burn patients are likely to be high in the setting of long-term opioid therapy and opioid tolerance. Patients on chronic opioid therapy have been found to have opioid requirements exceeding 4 times the amount used by an average patient. Intraoperative opioid administration should rely on a high dose of short-acting opioid on induction, followed by judicious administration of a long-acting opioid throughout the case. Ultrashort-acting opioids, such as remifentanyl, should be avoided due to increased likelihood of development of OIH. Short-acting opioids, such as fentanyl and alfentanil, can also be used either in bolus or infusion form during painful procedures and dressing changes.^{32,33} In patients with no IV access or in pediatrics, periprocedural intranasal fentanyl, midazolam, or dexmedetomidine administration may be considered.^{34,35}

INTRAOPERATIVE INFUSIONS

Ketamine

Ketamine is a phencyclidine derivative appreciated for its dissociative anesthetic, amnestic, and analgesic properties. As opposed to opioid analgesics, ketamine offers the advantage of preservation of airway reflexes and spontaneous respirations with concomitant analgesic benefit. At higher doses (1 mg/kg), ketamine may be associated with psychiatric side effects such as hallucinations and emergence delirium, as well as increase in secretions and sympathetic activation often resulting in tachycardia and blood pressure elevation. At lower doses (0.1–0.5 mg/kg or as an infusion 0.1–0.5 mg/kg/h) ketamine offers primarily analgesic benefits, with significantly decreased risk of psychiatric side effects such as bizarre dreams, mood alterations, and dysphoria. Psychotomimetic effects of ketamine can be ameliorated by concurrent administration of benzodiazepines or dexmedetomidine. Incidence of ketamine-related side effects is strictly dose-dependent and overall insignificant at the lower (analgesic) dose range. In the systematic literature review by McGuinness and colleagues,³⁶ among 67 participants, there was no report of ketamine-related hallucinations at infusion rates ranging from 0.15 to 0.3 mg/kg/h. A higher rate of ketamine infusion was associated with improved analgesic

outcome and reduction in primary hyperalgesia. Addition of morphine had an additive effect toward prevention of windup phenomenon.

Ketamine plays an important role in perioperative pain management by improving analgesia, decreasing opioid requirement, and prevention of opioid tolerance. Ketamine is also postulated to decrease risk of chronic pain development by enhancing spinal inhibitory pain pathways and inhibiting windup and central sensitization phenomena.³⁷ Ketamine is particularly effective in patients exhibiting poor analgesic response to opioids either due to opioid tolerance or OIH, and in patients with a strong neuropathic pain component.

Lidocaine

Although topical administration of lidocaine to burn patients remains controversial due to concern for systemic toxicity, in some studies IV lidocaine administration has been found to improve periprocedural analgesia.³⁸ Most of the available studies describe analgesic benefits as pertaining to visual analog scale scores alone, with no decrease in opioid consumption, improved anxiety, or patient satisfaction.^{39,40}

Dexmedetomidine

Dexmedetomidine is an alpha-2-adrenergic receptor agonist that has gained in popularity for its sedative, sympatholytic, anxiolytic, and analgesic properties that can be successfully used for periprocedural sedation in the burn injury setting. Dexmedetomidine is a useful adjunct to traditionally used medications such as benzodiazepines and opioids, and has a better side-effect profile with no evidence of tachyphylaxis or tolerance development with prolonged use. Dexmedetomidine can be associated with increased risk of hypotension and bradycardia.⁴¹

Although not a robust analgesic, in combination with other sedatives such as ketamine, dexmedetomidine contributes to improved sedation, hemodynamic stability, and overall tolerability of burn procedures. Dexmedetomidine has also been researched in pediatric burn patients because it can be successfully administered intranasally. Dexmedetomidine represents a safe adjunct alternative to opioids and benzodiazepines for periprocedural sedation.⁴²

Propofol

Propofol (2,6-diisopropylphenol) is among the most commonly used IV anesthetics used for periprocedural sedation. It is important to recognize that propofol, although a sedative, is devoid of

analgesic properties and attainment sedation with propofol is not suggestive of concomitant analgesia. Although widely used in sedation for adults, its use in young children remains off label due to persistent concerns of its potential unfavorable side effects of acidosis and myocardial dysfunction.^{43,44} Long-term infusions at doses exceeding 4 to 5 mg/kg/h should be avoided.

Benzodiazepines

Although devoid of analgesic properties, benzodiazepines are frequently used for sedation for their amnestic, anxiolytic, and sedative properties. Benzodiazepines may be administered IV, intramuscularly, by mouth, and even intranasally, which can be useful in pediatric burn patients.⁴⁵

Addition of benzodiazepines to opioid pain therapy has been found to improve analgesia and decrease opioid requirement.⁴⁶ Combination of benzodiazepines with opioids must, however, be used with caution because it increases the risk of respiratory depression and opioid-related risk of death.

INTERVENTIONAL BLOCKS

Some of the biggest challenges in burn pain management pertain to perioperative and periprocedural pain relief, in which sole pharmacologic therapy often proves inadequate. Recently, use of regional anesthesia for periprocedural burn pain management has gained in popularity.

Neuraxial analgesia, although a viable pain control option, is not commonly used in burn patients due to concern for risk of infection and coagulopathy often present in severely burned patients. Furthermore, in patients with a single limb burn, use of peripheral nerve blocks, as opposed to a neuraxial block, decreases risks and preserves mobility.⁴⁷

Regional anesthesia not only improves analgesic outcomes and patient satisfaction but offers safety resulting from avoidance of general anesthesia-related comorbidities. Regional blocks can be helpful in patients in whom opioid analgesics should be avoided (eg, severe pulmonary disease, obstructive sleep apnea). Patients with upper extremity burns may benefit from brachial plexus blocks (interscalene, supraclavicular, infraclavicular, axillary). Patients with lower extremity burns may benefit from lumbar plexus, femoral, or sciatic nerve blocks, or, if the injury is below the level of the knee, popliteal, saphenous, or ankle blocks.

Furthermore, placement of regional peripheral nerve catheters benefits the patient beyond the immediate perioperative timeframe. Peripheral

continuous infusion nerve catheters may be maintained for several days, thus providing pain relief for future surgeries and postoperative dressing changes alike.⁴⁸

Some of the most painful aspects of postoperative pain management in burn patients involve discomfort at the graft harvest site. In most cases, the graft tissue being obtained from the lateral thigh results in severe neuropathic pain in that area, often surpassing the pain of the burn itself. Two recent studies investigated use of regional anesthesia for management of postprocedural pain at the harvest site. Shteynberg and colleagues⁴⁹ described use of ultrasound-guided lateral femoral cutaneous nerve block for the lateral split-thickness skin harvest from the lateral thigh, resulting in up to 9 hours of improvement in pain. Cuignet and colleagues⁵⁰ investigated use of ultrasound-guided fascia iliaca compartment block followed by continuous ropivacaine infusion. The study showed statistically significant analgesic benefit, as well as decreased opioid requirement in the block patients as compared with controls.

Local Anesthetic Infiltration

Another option for the use of local anesthetics (LAs) for perioperative pain management is localized wound infiltration, most commonly performed with long-acting LA such as bupivacaine or ropivacaine providing the patient up to 8 hours of pain relief. Most recently, a multivesicular liposomal formulation of bupivacaine (Exparel) has been approved for a single-dose administration. Off-label use for peripheral nerve blocks and infiltrative blocks has also been described.^{51,52}

Outpatient pain care

Epidemiology Chronic persistent pain following burn injury is common in burn injury patients and it is estimated to affect 35% to 52% of burn victims.^{53,54} Inadequately treated pain is frequently associated with psychiatric comorbidities of depression, anxiety, and PTSD, and contributes to poor quality of life, increased health care resource utilization, and disability.⁵⁵

Pharmacologic outpatient management Pharmacologic management of chronic burn pain does not differ dramatically from the principles of pharmacotherapy for acute burn injury, with the goal of continued implementation of the principles of multimodal analgesia. Adequate acute pain control is of highest importance in an effort to prevent progression of acute pain to a chronic pain condition. Due to concern for development of central sensitization, tolerance, and OIH, use of opioid

monotherapy and excess opioid dose escalation should be avoided.

As a result of high, long-term IV opioid administration, burn injury patients often experience difficulty transitioning from IV to oral opioids and remain at potentially dangerously high levels of opioids at the time of discharge. Although opioid medications often remain the cornerstone of the immediate postinjury therapy, they should be weaned as the injury heals, with the focus being placed on utilization of neuropathic and adjuvant medications. Use of multimodal therapy, not only including adjuvant medications but also nonpharmacological measures, should be continued long term after hospital discharge. Multidisciplinary pain therapy should remain all-encompassing, including PT, occupational therapy, psychological counseling, and alternative therapies.

Opioid prescribing and the Centers for Disease Control and Prevention

If opioids are to be continued long term, ensuring proper opioid prescribing practices is of the highest importance. Inappropriate opioid dose escalation, lack of proper monitoring, and coprescribing with other sedatives is discouraged because it may lead to heavy opioid dependence, abuse, and potentially opioid-related death. The first steps to ensure safe opioid management should take place during hospitalization with a focus on assessment for opioid therapy suitability (eg, urine toxicology screen at admission, psychiatric history, prior history of drug use). Although opioid medications should never be withheld from an injured patient regardless of their opioid suitability, patients with prior history of abuse may necessitate additional treatment and thus should be identified early along the course of hospitalization. Second, at the time of discharge, patients should be provided with adequate but not excessive amount of opioid medications. The prescription should be in the amount sufficient only to the next follow-up visit and weaning parameters should be provided to the patient, if appropriate. Weaning parameters should be individualized to each patient depending on the degree and chronicity of the burn and burn-related pain. Weaning should not be initiated until the healing process of burns is complete. In most circumstances, opioid weaning by 10% weekly is considered quite conservative and should be well tolerated with little to no symptoms of opioid withdrawal.

If opioids must be continued for a long term, steps ensuring proper opioid utilization must be followed and may require patient referral to a pain management specialist.⁵⁶ The prescribing physician is obliged to discuss with the patient opioid treatment benefits, risks, goals, and

limitations. A plan for discontinuation of opioid therapy if it proves to be ineffective or unsafe should also be addressed. The patient's treatment goals must be specific and achievable, and reassessed frequently because they may change during treatment.

On completion of urine toxicology screen and proper assessment for the patient's suitability for chronic opioid management (expert psychological evaluation may be required in some cases), the patient and the treating physician should engage in a treatment agreement. Continuous pain psychology therapy and potentially repeat chronic opioid therapy reassessment is highly encouraged. At least annual urine toxicology screen and treatment agreement renewal is required. Medication-monitoring (pill counts) and controlled substance database evaluation should take place at least every 3 months.

Opioid therapy should only be continued if the patient meets established treatment goals in terms of pain control, functional improvements, and psychological well-being. Opioids should be avoided with other sedatives, especially with benzodiazepines, because coadministration of these medications has been found to significantly increase opioid-related deaths. Patients necessitating daily opioid doses in excess of 50 or more morphine milliequivalents (MME) per day should be prescribed naloxone rescue medication. If reasonable, the patient's daily opioid dose should ideally be maintained at or decreased to 90 or lower MME per day. Opioids should never be prescribed as a monotherapy. Use of adjuvant medications improves analgesic outcomes, decreases opioid requirements, and decreases opioid-related side effects, thus improving safety.

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