Pain and the Thermally Injured Patient—A Review of Current Therapies

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Thermally injured patients experience tremendous pain from the moment of injury to months or years after their discharge from the hospital. Pain is therefore a critical component of proper management of burns. Although the importance of pain is well recognized, it is often undertreated. Acute uncontrolled pain has been shown to increase the incidence of mental health disorders and increase the incidence of suicide after discharge. Long-term poor pain control leads to an increase in the incidence of persistent pain. Most burn centers have used opioids as the mainstay analgesic, but recently, the significant side effects of opioids have led to the implementation of new and combined therapeutics. Pharmacological agents such as gabapentin, clonidine, dexmedetomidine, and ketamine have all been suggested as adjuncts to opioids in the treatment of burn pain. Nonpharmacological therapies such as hypnosis, virtual reality devices, and behavioral therapy are also essential adjuncts to current medications. This review aims at identifying the currently available pharmacological and nonpharmacological options for optimal pain management in the adult burn population. (J Burn Care Res 2015;36:315–323)

Patients with burns experience pain from the moment of their injury and also throughout their rehabilitation. Some even continue to experience pain years postinjury. Although pain has been well recognized as an important component of the management of burns, it remains undertreated.[1–4] In fact, the literature suggests that burn pain is one of the most difficult to manage.[2,4–6]

Pain control is very important as inadequate pain control has short- and long-term consequences for the patients. Acute uncontrolled pain has been shown to increase the incidence of mental health disorders in patients (depression, posttraumatic stress disorder) and correlates with increased incidence of attempted suicide after discharge.[7,8] Poor pain control also decreases patient compliance with rehabilitation therapy and negatively affects the confidence of the patient in the burn team.[1,5] Thompson et al[9] showed that patient's discomfort during medical procedures impedes on wound care, increases the risk of wound infection, decreases the patient's ability to perform the usual range of motion exercises, increases psychological stress, and is associated with longer hospitalizations.

Long-term, repeated exposure to painful stimuli and prolonged acute pain leads to pain centralization and to an increased incidence of persistent pain.[1,10] Patients affected by persistent pain present a higher risk of depression and demonstrate suicidal ideation and anxiety.[1,10] Browne et al[10] surveyed 492 burn survivors and found that 18% reported persistent pain, 27% experienced depression, and 14% showed posttraumatic stress symptoms up to 11 years after the injury. Other studies have reported an even higher incidence (35–52%) of persistent pain postinjury. The mean total body surface area directly correlates with pain intensity.[10] In a study published by Browne et al,[10] patients who reported persistent burn-related pain were often the ones reporting depressive and posttraumatic symptoms. Patients who recalled high levels of acute pain were also the ones who reported chronic burn pain.[10] Long-standing pain affects patients' lives and strongly correlates with disability, poor quality of life, relational problems, and higher

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health care use.[11] These findings all emphasize the importance of proper management of acute pain in order to optimize care in hospital, decrease the incidence of mental health disorders, and prevent development of persistent burn pain.

PATHOPHYSIOLOGY OF PAIN

An understanding of the pathophysiology of burn pain can help in its management. Injuries caused by thermal burns immediately cause pain because of the stimulation of local skin nociceptors. Pain is conducted along three neuronal pathways from the periphery to the cerebral cortex. First-order neurons transmit nociceptive signals through Aδ and C fibers to the dorsal horn of the spinal cord.[1,12,13] Neurotransmitters such as glutamate, substance P, and calcitonin gene–related peptides are released in the dorsal horn and activate the second-order neuron.[13] This neuron crosses to the contralateral side of the spinal cord and ascends in the spinothalamic tract till it reaches the thalamus.[13] The activated third-order allows for perception of pain through its signal in the somatosensory cortex.[13]

In the periphery, the release of neurotransmitters leads to the "axon reflex," redness, swelling, and tenderness at the site of injury.[13] In parallel, an inflammatory response is initiated within minutes of the injury, leading to the release of chemical mediators. Both the neurotransmitters and the chemical mediators sensitize and stimulate the active nociceptors at the injured site, which increases sensitivity and is known as primary hyperalgesia.[1,2,13,14]

Nociceptive afferent fibers are continuously and repeatedly stimulated causing an increase in dorsal horn excitability, especially through the N-methyl-D-aspartate (NMDA) receptor, causing an increase in sensitivity of the surrounding undamaged skin, known as secondary hyperalgesia.[1,2,13] This central sensitization leading to secondary hyperalgesia may become irreversible and may cause chronic pain.[8,14]

In addition to the local nociceptive response, the thermal injury causes systematic changes in both pharmacokinetics and pharmacodynamics during the acute phase of the burn.[3,15] During the first 48 hours after the injury, the blood supply to the body organs is decreased.[1] This decreased perfusion causes a reduction in drug clearance. After the first 48 hours, a hypermetabolic phase ensues causing an increase in drug clearance.[1] Plasma protein levels are also affected by thermal injuries. Often, plasma protein levels are reduced, causing a decrease in the fraction of protein-bound drug and therefore an increase in the level of free, unbound drug.[1] The increase in free, active drug is difficult to predict, which adds to the challenge of pain management.[15] Because of the unpredictable effect of analgesics in the acute phase, pain-scoring systems should be used to monitor the efficacy of analgesics in thermally injured patients.

PAIN ASSESSMENT

The pain experienced by each patient varies tremendously and commands personalized pain-assessment tools. Assessment of pain requires inquiring about the nature of pain, site of pain, aggravating and alleviating factors, and a description of the pain.[1,16] The quality of the pain experienced by the patient is important to determine as patients experience different types of pain.[1] During the acute phase, patients experience constant dull pain because of injury to the tissues as well as anxiety related to their illness and immobility.[2,12] This is background pain. Pain related to wound cleaning, dressing changes, debridement, line insertions, and physical activity is termed procedural pain. This type of pain is described as being of high intensity and short duration.[2,12] Because of the pain associated with procedures, patients can experience anxiety and psychological distress in anticipation to these events.[17] Over time, anxiety associated with procedures can increase in intensity.[17] Patients also experience unpredictable surges of pain throughout the day, which is considered breakthrough pain and they will also experience postoperative pain.[1,2,12,18] As tissue regenerates, an intense discomfort can be felt by the patient, which is best described as tingling or itching sensation.[14] After the wounds have healed, burn patients could experience neuropathic pain. The International Association for the Study of Pain defines it as "pain initiated or caused by a primary lesion or dysfunction in the nervous system."[19] It has been described as burning, "stabbing, shooting, pins and needles, and electric shock-like sensations."[20]

During the hospitalization, examination of the painful area may sometimes suggest a cause such as wound infection, tight dressing, tissue edema, or regenerating tissues.[1] In order to trend the pain and facilitate its assessment, several scoring systems have been developed.[1,8] Pain can be qualified through adjective scales where patients are asked to select a word (none, mild, moderate, severe) to describe their level of pain.[1] Numerical scoring systems (scales from 0–3 or 0–5 or 0–10) are also used for a more quantitative assessment.[1] Another method is the visual analog thermometer where the patient moves a strip between "no pain" and "unbearable pain." This method has been validated as both sensitive and useful in pain assessment.[1] For pediatric patients, pictorial representation scales are usually more accurate.

In critically ill patients, several other scoring systems have been developed in communicative as well as noncommunicative patients: the Pain Assessment and Intervention Notation algorithm, the Nonverbal Pain Assessment Tool, the Adult Nonverbal Pain Scale, the Behavioral Pain Scale, and the Critical Care Pain Observation Tool.[6,16] These scoring systems use a combination of behavioral and physiological parameters to assess pain. Behavioral cues used are movement/activity, facial expression, and posturing/guarding.[16] Physiological parameters indicative of pain are increased heart rate, respiratory rate, and blood pressure as well as perspiration or pallor.[16] All these different methods of assessment allow quantification as well as trending of pain.

PAIN MANAGEMENT

Pain is modulated both endogenously through endogenous opioids and exogenously through the pain regimens given to the patient by the treating team. Pain is modulated endogenously by the neural system through opioid peptides, specifically, met-enkephalin, leukenphalin, β-endorphin, and dynorphin, which bind to μ (mu), δ (delta), and κ (kappa) receptors.[12,13] The internal modulation varies from patient to patient and is only one of the factors that affect pain perception. Other factors that will modulate the patient's personal perception of pain include genetic predisposition, history of substance abuse, personality type, patient's expectations, cultural beliefs, past experiences, relationship between the patient and the burn unit staff, patient's mood (anxiety, depression), burn wounds characteristics (size, severity of burn, stage of burn healing), and analgesics used.[1,2,9,12] The combination of these factors makes the pain experience unique to each thermally injured patient.

Each burn center uses a variety of combination of medications and psychological therapies to achieve pain control in burn patients. Opioids are the mainstay analgesics; fentanyl, sufentanil, and morphine are the three most commonly used.[18] Opioids have the potential of causing hyperalgesia through central sensitization and therefore other pharmacological agents such as acetaminophen, lidocaine, clonidine, gabapentin, and ketamine have been suggested as adjuncts in the treatment of pain.[1,21] Nonpharmacological therapies are an essential component of pain management; massage, hypnosis, and psychological therapies have all been shown to improve the patient's outcomes.[2] In fact, Berger et al[7] achieved better pain control, reduced analgesic requirements, reduced anxiety, and improved wound healing by combining hypnosis with pharmacological agents.

This wide variability of pain-management protocols results from the lack of consensus and guidelines on optimal practice of analgesia and sedation in burn patients. Trupkovic et al,[18] who surveyed 43 burn centers in Europe, reported that two thirds of responders were dissatisfied with their strategies to manage sedation and analgesia of burn patients.

PHARMACOLOGICAL THERAPY

Opioids

Opioids mimic the effects of endogenous opioid peptides by interacting with the μ, δ, and κ receptors (Figure 1).[22] Each medication has a different effect on these subtypes of receptors, but most activate the μ receptor.[23] Opioids also cause cellular hyperpolarization by closing the N-type voltage-operated calcium channels and by opening calcium-dependent potassium channels. This Hyperpolarization Decreases Neuronal Excitability and therefore decreases pain response.[22] Opioids also decrease intracellular cyclic adenosine monophosphate (cAMP); this modulates the release of nociceptive neurotransmitters such as substance P.[22]

Opioids are the cornerstone of burn pain management and are potent analgesics. Certain opioids have been shown to have specific beneficial effects; for example, morphine has been shown to reduce posttraumatic stress disorder symptoms.[1] Although opioids provide excellent analgesia, they do not prevent the development of central pain sensitization.[1]

Side effects of opioids are significant; these include respiratory depression, constipation, sedation, pruritus, sleep cycle interference, nausea, and vomiting.[14,23–25] A controversial side effect of opioids is their potential association with immunosuppression. Some experimental studies have shown that opioids induce immunosuppression, leading to infections such as pneumonia.[24] Rittner et al[24] reviewed data in the intensive care setting and concluded that the evidence was unclear as to the link between infection and opioid use. Evidence was contradictory in the postoperative care setting.[24] Rittner et al finally concluded that further studies were necessary to investigate opioid-induced immunosuppression.

Opioids are also associated with the development of tolerance. Over time, increasing doses of opioids are needed to achieve the same analgesic effect.[1,14] Changing the opioid can restore analgesia in tolerant patients. Methadone has also been used with success in certain patients.[1] Patients can also become dependent on opioids with long-term use.[14]

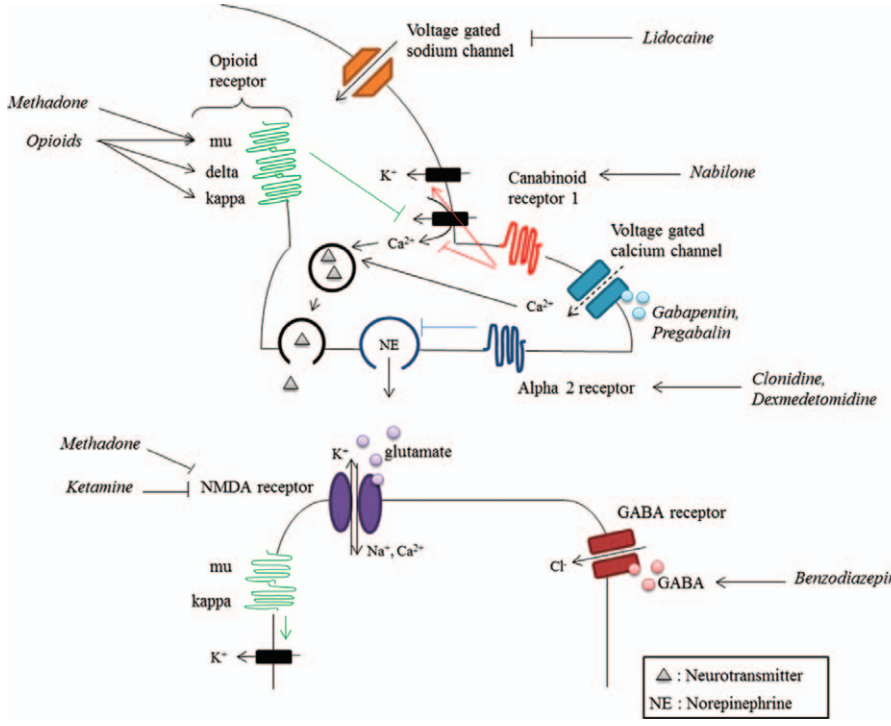

Figure 1. Site of action of pharmacologic agents. *GABA*, γ-aminobutyric acid; *NMDA*, N-methyl-D-aspartate.

Opioids can also induce hyperalgesia through activation of pronociceptive processes in afferent neurons and in the spinal cord.[14] Increasing doses of opioids worsens opioid-induced hyperalgesia (OIH). Therefore, the first step in treatment of OIH is to decrease the dose of opioids.[14] Another strategy is rotating opioids, methadone being the suggested replacement medication. Last, the use of adjuvant drugs, which decreases the need of opioids, has been suggested for the treatment of OIH. NMDA receptors have been implicated in the development of OIH. Ketamine is hence effective in treatment of pain in patients with OIH.[14] Other adjuncts such as NSAIDs, clonidine, dexmedetomidine, and gabapentin can also be used.[14]

Nonopioid Adjuncts

Acetaminophen. Acetaminophen is an antipyretic and an analgesic with both central and peripheral pain modulation activity.[26,27] The mechanism of action of acetaminophen is unknown, but it may involve the inhibition of central prostaglandin synthesis, the activation of descending serotonergic pathways, and the inhibition of cyclo-oxygenase 2 activity.[22,26] It can be administered as a first-line treatment of minor burns and as an adjunct to opioids for major burns as it has a synergistic effect.[1]

Nonsteroidal Anti-Inflammatory Drugs. Nonsteroidal anti-inflammatory drugs (NSAIDs) are analgesic, anti-inflammatory, and antipyretic medications by reversibly inhibiting cyclo-oxygenase, by inhibiting prostaglandin production, and sometimes by inhibiting the lipoxygenase pathway.[22,23,28] These drugs are effective as adjuncts to opioids as they decrease central hyperalgesia, have a synergistic effect, and are opioid sparing.[1,12,23] NSAIDs have several side effects that limit their use in major burns: 1) stomach irritation and ulceration, 2) platelet dysfunction, 3) altered renal function that can lead to renal failure, and 4) alteration of concentration of protein-bound medication such as warfarin.[12]

Mu-Opioid Agonist and NMDA Antagonist

Methadone. Methadone is a synthetic μ opioid receptor agonist that has weak NMDA receptor antagonistic activity.[1,5,29–31] Methadone is a potent analgesic, is an effective alternative analgesic in opioid-tolerant patients, is used to treat opioid dependence, and can also attenuate central sensitization.[5,29,30,32]

Jones et al[5] suggested that early use of methadone leads to better outcomes for burn patients. In fact, in a retrospective pilot study, Jones found that mechanically ventilated patients who received early methadone treatment had an increase in the number of ventilator-free days. Further studies are necessary to confirm this finding.

1NMDA Receptor Antagonist

Ketamine. Ketamine is a dissociative anaesthetic when used at doses greater than 1 mg/kg.[1,33] At

lower doses of 0.1mg/kg, ketamine is an effective analgesic for patients exhibiting a poor response to opiates.[1] Ketamine acts on the thalamic function and on the limbic system as a potent noncompetitive NMDA receptor antagonist and inhibits central pathways associated with central pain sensitization (Figure 1).[2,25,33,34]

Ketamine is widely used in burn patient care because of its pharmacological profile: it is catecholamine-sparing and is an effective analgesic against 1) neuropathic pain, 2) opioid-induced hyperalgesia, and 3) secondary hyperalgesia.[18,34] Ketamine reduces opioid requirements by 30% in the postoperative period when used at a dose of 0.1 mg/kg.[1,25] Ketamine preserves cardiovascular stability, promotes gut motility, and maintains spontaneous breathing.[1,18,34]

Ketamine use is limited by its side effects, specifically its sympathetic activation leading to increased heart rate and systolic blood pressure. Sympathetic activation resulting in an increase in salivation has been reported to cause laryngospasm in 0.4% of patients.[1] Ketamine may cause psychomimetic side effects (hallucination, delirium).[1,34,35] Studies have suggested decreasing the dose of ketamine used or combining ketamine with other analgesic or sedative agents to decrease these side effects and dose requirements of ketamine.[1,2,18,35] MacPherson et al [35] combined benzodiazepines and ketamine in a patient-controlled analgesic device and observed good pain control with minimal side effects when the device was used during procedures.

Benzodiazepines. Benzodiazepines are anxiolytics used as adjuncts in the treatment of burn patients. They are not analgesics, but do reduce the perception of pain in anxious patients.[1] Benzodiazepines act by amplifying γ-aminobutyric acid in the central nervous system, and by reducing catecholamines in the peripheral nervous system (Figure 1).[36] Benzodiazepines have many side effects including respiratory depression, physiologic addiction, and rapid development of tolerance.[36] Benzodiazepines need careful monitoring when used, but are effective adjuncts to opioids as they decrease distress in burn patients.[36]

Gabapentin. Gabapentin is a structural analog of γ-aminobutyric acid, which is used as an antiepileptic as well as in the management of neuropathic pain.[1,37–39] Its mechanism of action is not fully defined, but it involves inhibition of the release of excitatory neurotransmitters and increases the release of inhibitory neurotransmitter γ-aminobutyric acid by binding to the α2δ-1 subunit of the voltage-gated calcium channel.[38,40] Gabapentin acts both centrally and peripherally. Gabapentin has been used to manage persistent burn pain because it inhibits the central sensitization of pain, binds to presynaptic calcium channels involved in pain hypersensitivity, and indirectly inhibits overactivation of the NMDA receptor.[1,39] It has recently been suggested as first-line therapy for the management of neuropathic pain.[38]

Gabapentin has been shown to relieve postburn pruritus and recent studies have recommended its use even in patients responsive to antihistamines.[37,41]

Gabapentin's use in the acute burn pain setting is controversial. A case series of six patients suffering from neuropathic pain poorly responsive to opioids reported that gabapentin when given in the acute setting led to a rapid resolution of neuropathic symptoms.[42] A case-control study reported a reduction in morphine requirements when gabapentin was used as adjunct in the acute setting.[1,43] A recent study published by Wibbenmeyer et al[44] demonstrated the contrary; it reported that no opioid-sparing effects were seen with administration of gabapentin in the acute phase. Even though gabapentin appears to have certain beneficial effects in reducing opioid requirements, providing neuropathic pain control and aid in relief of pruritus, the timing of its administration needs to be further studied.

Pregabalin. Pregabalin is an antiepileptic drug with both analgesic and anxiolytic properties. Like gabapentin, it binds the α2δ-1 subunit of the voltage-gated calcium channel.[19] It is currently used for the treatment of diabetic and postherapeutic neuropathic pain as well as for partial seizures.[20] Side effects of pregabalin are dizziness, somnolence, dry mouth, and edema.[20] In a retrospective chart review, Wong et al[20] found that patients treated with pregabalin for neuropathic pain had a 69% reduction in pain with few side effects. Gray et al[19] confirmed the benefits of pregabalin in a randomized, double-blind, placebo-controlled trial.

Alpha-2 Agonists

Clonidine. Clonidine is an α-2 agonist used for its sedative, anxiolytic, and analgesic properties (Figure 1).[45] Analgesia occurs by stimulating the central descending inhibitory system, by recruiting neuromediators that modulate pain perception and by inhibiting substance P release.[12] Clonidine can be used as single agent for analgesia, but has been associated with hypotension.[46] Clonidine is useful as an adjunct as it enhances opioid analgesia, decreases opioid requirement, and prolongs local anesthetic action.[1,45–47] It can also be administered in the management of alcohol, opiate, and nicotine withdrawal.[1,45]

In the critical care setting, Pichot et al[48] found many beneficial effects of clonidine: sedation combined with arousability, preservation of respiratory drive, improvement of left ventricular performance,

suppression of delirium, reduction of protein metabolism, preservation of renal function, and improvement of tissue perfusion. In order to obtain such beneficial effects, clonidine was administered as a slow intravenous infusion with avoidance of boluses.[48]

Dexmedetomidine. Dexmedetomidine is an α-2 agonist used as a sedative with mild to moderate analgesic properties.[48] Dexmedetomidine has specificity to the 2A subtype of the α2 receptor, causing it to be a more effective sedative and analgesic than clonidine.[49]

Dexmedetomidine also reduces the requirement of anesthetics, sedatives, and analgesics.[2,50,51] Dexmedetomidine has been reported to decrease respectively opioid and propofol requirement by 50 to 60% and 86%.[2,50] Dexmedetomidine is a good adjunct to ketamine as it attenuates ketamine-induced cardiac stimulation and prevents delirium.[1]

Cannabinoids

Nabilone. Nabilone is a synthetic cannabinoid receptor 1 agonist (Figure 1).[52,53] Nabilone has been used as an antiemetic in patients receiving chemotherapy, and recently has been used for the control of neuropathic pain.[53–56] The mechanism of pain modulation by nabilone is complex and involves the peripheral afferent nerves, the dorsal root ganglia, and spinal dorsal horn as well as specific brain areas.[52,54] Bestard et al [52] studied the effectiveness of nabilone as compared with gabapentin on neuropathic pain and concluded that nabilone is effective at decreasing pain and anxiety as well as improving sleep.

Nabilone's common side effects are lightheadedness, dizziness, anxiety, memory impairment, speech impediment, and sedation.[52,54,57] Studies recommend starting patients with low doses of nabilone in order to avoid disabling side effects and titrating the medication with gradual dose increases over time.[54,58] Nabilone is not considered first-line adjunct therapy but can be considered as adjunct therapy in the difficult-to-treat cases or those with history of cannabis use.

Lidocaine. Lidocaine is an anti-inflammatory medication, which can be used as a local, topical, or systemic anaesthetic. Lidocaine acts on the voltage-gated sodium channels by blocking the inflow of sodium, causing an inhibition in the propagation of the action potentials in neurons (Figure 1).[59]

The use of topical lidocaine gel in burn pain management is controversial. Harmful side effects have been reported when lidocaine has been applied directly onto mucosal membranes, leading to rapid systemic absorption and subsequent toxicity.[12] Topical application has also been associated with seizures in children.[12] Brodfeldt et al[12] showed that 5% cream applied at a dose of 1 mg/cm^2 offered analgesic effect for up to 4 to 6 hours without systemic toxicity.

Lidocaine has also been found to be useful when used intravenously as an infusion.[12] A prospective, double-blind, randomized study by Wasiak et al[60] compared intravenous lidocaine with placebo in 45 patients and found that verbal rating scales were lower in patients treated with lidocaine. No effects on opioid consumption, anxiety levels, or patient satisfaction were reported.[60] A Cochrane Review in 2012 concluded that although the subjective pain ratings from the previous study were optimistic, further well-designed clinical trials are necessary to determine the effectiveness of lidocaine.[1,61]

Lidocaine may play a role in decreasing edema formation in burns and may reduce anxiety because of the medication's euphoric effects.[12]

NONPHARMACOLOGICAL THERAPY

Factors such as depression or anxiety strongly affect the perception of pain in burn patients. A multidisciplinary approach to the management of burn pain is strongly recommended. Although pharmacological agents targeted to control pain are important, nonpharmacological therapies are essential adjuncts for optimal pain control.

Cognitive, preparatory, behavioral, and hypnotic therapies have all been shown to help patients manage their pain.[12] Cognitive interventions address the thoughts of the patient by either teaching them avoidance techniques (eg, mental imagery, self-talk) and/or reappraisal techniques (reconceptualizing the sensory information in a more positive context). Preparatory interventions focus on informing the patient about expectations both from the procedure (details of the intervention) and from sensorial perception (what the patient is likely to feel during the procedure). Behavioral interventions provide patients with tools to cope with pain, such as relaxation training and reinforcement training (eg, pain medication given as a reward for a patient reporting pain during a nurse visit as well as congratulating the patient after successfully completing a procedure).[12] Massage, therapeutic touch, and music therapy can also help reduce pain.[18] Hypnosis has been shown by Berger et al[7] to improve pain control and reduce anxiety when combined with pharmacological agents. Berger et al found that patients treated with this combination had reduced needs of grafting and had shorter hospital admissions.

Other nonpharmacological therapies, such as multimodal distraction device, which is a hand-held technology, have been developed for pediatric patients to reduce distress and pain during procedures.[62,63] Miller et al[63] showed that multimodal distraction combined with procedural preparation reduced the pain and distress experienced by children during procedures and decreased the length of treatment.

Virtual reality (VR) is another form of distraction; it is a technology that immerses the user into a computer-generated environment.[64,65] A pilot study by Morris et al[64] found this device to be a safe, low-cost, effective adjunct therapy in the pain management of burn patients. Hoffman et al[65] confirmed these findings in their study by showing that VR reduced pain during procedures and physical therapy and alsoreduced fear and anxiety in pediatric patients. Kipping et al[66] compared VR with standard distraction in a randomized controlled trial in adolescents and did not find a reduction in pain level or length of treatment. This study did find that fewer rescue doses of Entonox were given to VR patients as compared with doses given to standard distraction patients.[66] A case report suggested that the combination of VR and ketamine is an effective analgesic regiment for burn wound cleaning.[25] Further studies are necessary to better understand the role of devices as single agents or adjuncts to either pharmacological agents or psychological therapy in the management of burn pain.

CLINICAL PRACTICE

The initial approach to a thermal burn injury is to assess airway, breathing, and circulation.[67] Once these have been managed, the burn injury should be assessed through percentage of total body surface area, degree of burn injury, and patient characteristics (age, comorbidities). This assessment allows for some prediction of the pain intensity. Analgesia can then be initiated based on this predicted pain level.[67] Another method of treatment consists of following the analgesia ladder: step 1, nonopioids (acetaminophen, NSAIDs); step 2, mild opioids (codeine); step 3, strong opioids (morphine).[15,68]

In acute mild burn pain, patients should be prescribed acetaminophen regularly if they do not have contraindications to this medication.[68] NSAIDs should be added to acetaminophen, but should be prescribed with caution in the patient with shock or in the elderly.[67] For moderate to severe acute burn pain, opioid can be administered as adjuncts to acetaminophen and NSAIDs. Laxatives, antiemetics, and opiate antagonists (eg, naloxone) should concurrently be prescribed to prevent and control opioid related side effects.[68] Several routes of opioid administration have been suggested to control background pain: orally (short-acting agents: oxycodone, hydromorphone, codeine; long-acting agents: sustained-release morphine or hydromorphone, sustained-release oxycodone, methadone), transdermally, intramuscularly, through a patient-controlled analgesia device, and intravenously (bolus or continuous infusion of morphine or fentanyl).[15,67,69]

Breakthrough pain must also be addressed at admission. Opioids should be prescribed as required to control this type of pain.

The next type of pain to address is procedural pain. For minor procedures such as small wound dressings, a bolus of opioids or local anesthesia can be used. Alternatively, conscious sedation can be used; a combination of midazolam and an opioid (fentanyl, alfentanil) is effective.[67] The opioid can be given either by the physician or by a patient-controlled device, which has been shown to give patients a sense of control and a higher level of satisfaction with their pain treatment.[70] For more extensive procedures such as debridement and long dressing changes, deep sedation with combination of a benzodiazepine (eg, midazolam) and ketamine or propofol combined with an opioid or even general anesthesia is recommended.[67,71]

Procedural pain is also associated with anxiety and distress, which increases the amount of pain experienced by the patient.[17,71] Benzodiazepines, propofol, or ketamine can be used to decrease anxiety. Of note, these agents only reduce psychological distress and should be combined with an appropriate analgesic.[71]

Nonpharmacological approaches are indicated as adjuncts for procedural pain. Distraction techniques, hypnosis as well as specific devices can all be used during procedures to improve pain management. Relaxation, cognitive behavior therapy, and scheduling of treatments can improve anxiety-related pain.[71]

In the postoperative period, background pain may worsen. The baseline pain medications of the patient should therefore be reviewed after the operation and frequency of administration of analgesics should be increased to prevent inadequate pain control.[69] Because donor sites are significant sources of pain, regional nerve blocks can be performed. Lateral femoral cutaneous nerve block can provide anesthesia to lateral thigh donor sites.[70] Fascia iliaca compartment block provides anesthesia to both the lateral femoral cutaneous nerve and the femoral nerve distribution, but this type of block is associated with risks of muscular weakness and overdose.

All these initial pain regimens must be reassessed on a daily basis depending on the pain scores of the patient and the need for rescue medication. Patients' satisfaction, preferences, and side effects of medications are to be taken into consideration when adding or modifying a pain regimen.[4]

After the acute management of pain, the presence of chronic pain or neuropathic pain should be assessed.[17] A study in Germany by Dauber et al[72] found that 52% of the 348 patients surveyed reported pain 12 years after their injury. Gabapentin, pregabalin, ketamine, and nabilone are some of the pharmacological options available for the treatment of chronic neuropathic pain.[4,20]

CONCLUSION

Pain management is a significant component of care provided to the thermally injured patient. Patients' personal factors such as past experiences, genetic predisposition, personality type, level of anxiety, mental health disorders, and burn wound characteristics make the pain experience unique to each patient. This high variability between patients demands personalized pain-assessment tools. Burn unit staff must inquire about pain during their assessments and if present, qualify, quantify using adjective or numeral scales, and examine the painful area. The patient's treatment should be revised based on these assessments. Inadequate pain control has short- and long-term sequelae. Acute uncontrolled pain has been shown to increase the incidence of depression and posttraumatic stress symptoms, decrease patient compliance with rehabilitation therapy, and negatively affect the trust of the patient in the burn team, and can lead to an increase in the incidence of persistent pain in the long-term. By correctly identifying pain, burn teams can adjust pharmacological and nonpharmacological therapies to optimize pain management and prevent the short- and long-term consequences of poor pain management.

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