The Complexity of Managing Pain in Burn Patients: A Review of Current Therapies

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ABSTRACT

Burn injuries requiring medical treatment are very common, devastating, and painful. Pain management in burn patients has been a great challenge for many years. Unfortunately, inconsistent and outdated practices are still reported in the literature, mainly due to a lack of data supporting high-level evidence-based standards of care. Many studies have shown how inadequate and undertreated pain management is detrimental to burn patients. In general, pain management requires a comprehensive understanding of the complex physiology and dynamic pharmacokinetic changes occurring in the patient. Pharmacologic therapy can alleviate pain, and nonpharmacologic treatment may provide improved pain control as an adjunct; thus, using both can provide greater analgesia. By meeting the goal of alleviating pain and creating an environment that is less stressful for our patients, we will also achieve greater adherence to the follow-up and treatment of these wounds, which also leads to less risk of infections. This article reviews recent literature on pharmacologic and nonpharmacologic strategies to manage burn pain.

KEY WORDS: *Burn pain management, Multimodal approach, Nonpharmacologic treatment, Pharmacologic treatment*

INTRODUCTION

Burn patients experience a considerable amount of pain. One patient can present different burn depths; deeper, full-thickness burns are less painful than superficial and partial thickness burns because of afferent nerve destruction; second-degree burns are hurtful, with even changes in the air current passing the exposed injured skin or changes in temperature causing excruciating pain.[1,2] However, severely burned patients, in addition to the psychological and physical distress, also go through daily painful experiences from therapeutic procedures, causing pain that is similar to or even worse than the one elicited by the injury itself.[3]

Many definitions of pain have been proposed over the years; however, in 2020, the International Association for the Study of Pain (IASP) revised its globally accepted definition for the first time since 1979, describing pain as a biological, psychological, and social experience that varies among individuals, not always associated with tissue damage, and taking into consideration those who are not capable to verbalize their pain experiences. Although the biopsychosocial phenomenon of pain is complex and not fully understood, it has been well-described how burn pain includes nociception, primary (in tissues directly damaged by the burn) and secondary (tissues adjacent to the burn) hyperalgesia, and neuropathy.[4] However, the perception of pain is a personal experience, and burn pain management is challenging, arising from the moment of injury through rehabilitation and beyond. Thus, it requires a multidisciplinary approach, making individualized management necessary.

Despite current developments in burn pain management, inconsistent and outdated practices are still reported in the literature. Many studies have shown how inadequate and undertreated pain management is detrimental to burn patients. Patients show increased depression, posttraumatic stress disorder, and suicide risk, as well as decreased compliance with rehabilitation, which affects wound healing.[5-7]

Although some guidelines are available, there is no standard of care for burn pain management.[8-10] More educational efforts are necessary to improve pain management in patients with burns. Routine pain evaluation is mandatory for

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ACKNOWLEDGEMENTS: The authors have not received any funding or grants in support of the presented research or for the preparation of this work and have no declarations of potential conflicts of interest.

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Burn Care and Prevention 2022/4: 124-131

efficient and safe analgesia, and a multidisciplinary approach with pharmacological and nonpharmacological therapies is crucial to minimize adverse effects. Pharmacological therapy with opioids and nonopioids is the mainstay for analgesia, but not all patients respond satisfactorily to this treatment. Pharmacological therapies are not enough to treat the psychological and emotional components of pain; thus, nonpharmacological techniques are useful adjuncts, especially during the emerging opioid epidemic faced by many countries.[8,10,11]

This review aimed to provide an overview of the most common pharmacologic and nonpharmacologic approaches to treating burn pain.

Pain Assessment

Pain will vary with burn depth (Table 1). It is essential to perform a multidimensional pain assessment to determine the treatment plan. Pain assessments should be conducted and recorded by physicians or nurses several times daily; during all phases of care; and before, during, and after procedures and administration of treatment, particularly to address background and acute pain.[1,2,10] Each tool has a specific clinical scenario to be applied throughout the different phases of care. Some good pain assessment tools are verbal adjectives, numeric rating scales, numeric rating scales translated into word and behavior scales, and visual analog scales that have undergone repeated validation and performed well in different patient populations, although these scales have not been validated in the burn population. The visual analog and numeric rating scales are the most used in adults; populations who are unable to communicate present challenges, and observational scales and physiologic indicators such as heart rate and blood pressure should be used.[10-14] The Critical Care Pain Observation Tool is a behavioral pain scale recommended for nonverbal critically ill adults, and the Burn Specific Pain Anxiety Scale (BSPAS) is a self-reporting scale recommended to assess pain-related and anticipatory anxiety.[10,14-16]

Burn Pain Paradigm

Patterson's burn pain paradigm is a useful tool for pain management that considers different phases and pain variabilities. The paradigm-based management serves as a guide for the use of analgesics and classifies burn pain into 5 different phases: background, breakthrough, procedural, postoperative, and chronic pain (Table 2).[8,17-20]

Pharmacologic Management

Pharmacologic treatment must be individualized to consider the patient's comorbidities, current medications, general conditions, respiratory function, and burn severity. For years, opioids have been considered the first-line treatment for acute burn pain, but they often cause unwanted side effects or tolerance issues. It would be ideal to achieve the desired level of pain control by decreasing the use of opioids with the use of nonopioid drugs.[9-11,20] The superiority of opioids over nonopioid therapy for burn pain has never been demonstrated in trials, and the drugs and techniques for analgosedation are determined according to provider preferences.[20]

Opioid analgesics

Opioid analgesics are inexpensive and widely available; in many cases, they are the mainstay of pain management. Opioids act by closing presynaptic calcium channels and opening postsynaptic potassium channels, thus reducing synaptic transmission. They can be administered intravenously, orally, transdermally, sublingually, and rectally, with delivery via oral and intravenous being the ideal routes. Pharmacokinetic changes have been documented for morphine, fentanyl, and propofol due to the hypermetabolic response to burns.[9-11,21] Patients are treated individually based on the severity of the burns, and physicians must continuously perform pain assessments to adjust the dosing depending on the patient's response to pain. Careful monitoring is required due to the potential development of physiological tolerance, dependence, and addiction.

TABLE 1. Pain Variability According to Burn Depth

Type of Burn	Burn Depth	Pain Sensation	Pain Features
A	Superficial Erythema Blisters	 + ++	 Painful Severe pain to touch
AB	Deep Dermal	+/-	Decreased pain sensation to touch but present to deep pressure
B	Full-thickness	Absent	Painful to deep pressure and in edges and surrounding areas if affected by type A or AB injuries
C	Tissues under skin destroyed	Absent	Pain to deep pressure in the burned area and in surrounding areas if affected by type A or AB injuries

It is hard to determine an appropriate dose–effect relationship for opioids.[21] During the "ebb phase" of the hypermetabolic response to burns, patients experience hemodynamic changes, especially from intravascular volume depletion.[22] With these pathophysiological changes, high doses of opioids are used, worsening these changes and blunting the response to fluid resuscitation and leading to excessive volume resuscitation, a phenomenon known as "fluid creep." A balance between the dose of opioids given and the potential for exacerbation of hemodynamic changes must be achieved.

Patient-controlled analgesia (PCA) with intravenous opioids is safe and efficient. The mainstay of PCA is to maintain adequate plasma concentration of opioids. The use of PCA with intravenous morphine, hydromorphone, or another opioid can be used to achieve faster effects with decreased daily medication requirements. It is necessary to educate patients on the common side effects, including constipation, sedation, nausea, and respiratory depression. The use of opioids combined with nonopioid and nonpharmacological measures is recommended. Many countries are facing an opioid epidemic due to misuse and overdoses, and numerous hospitalized burn patients are still receiving a high amount of opioids ("opioid creep").[21,23-25]

Nonopioid analgesics

Acetaminophen: There are not many studies conducted on burn patients; however, acetaminophen has been regularly used in this population, and its mechanism of action has yet to be defined. Acetaminophen is effective as an analgesic and antipyretic with appropriate dosage (not to exceed 4 g/day). Hepatotoxicity is a concern; thus, acetaminophen should be used cautiously in patients with liver disease.[9,10,19,24]

***Nonsteroidal antiinflammatory drugs*:** Ibuprofen, naproxen, ketorolac, and diclofenac are the most commonly used nonsteroidal antiinflammatory drugs (NSAIDs) in burn patients. These drugs act by inhibiting COX1 and COX2 and blocking prostaglandin synthesis. Nonsteroidal antiinflammatory drugs are analgesic, antipyretic, and anti-inflammatory. It is important to bear in mind concerns about skin graft take and hematoma and renal, gastrointestinal, and hematologic side effects. COX inhibitors like celecoxib are recommended in patients with gastrointestinal bleeding and ulceration.[9,10,19,25]

***Ketamine*:** Ketamine is a noncompetitive N-methyl-d-aspartate receptor antagonist with a rapid onset of action and a unique characteristic of inducing narcosis, analgesia, and amnesia simultaneously. It can be administered intravenously or intramuscularly for procedural sedation; at a low dose, ketamine can be used as an adjunct to opioid therapy postoperatively and is also recommended in patients with opioid tolerance.[9,10,19] Although it rarely induces bronchospasm and does not cause hypotension, appropriate training for the staff and monitoring are required. Coadministration with a low-dose benzodiazepine reduces the incidence of hallucinations.[9,10,26]

TABLE 2. Burn Pain Pharmacotherapy Approach Following the Burn Pain Paradigm

Phase of Pain	Pain Features	Suggested Therapy
Background	Long duration, constant ("always present"), dull pain at rest, low to moderate intensity	Opioids, nonsteroidal antiinflammatory drugs, distraction techniques
Breakthrough	Short duration, rapid onset/offset (spiking), intermittent, sometimes excruciating; occurs when analgesic effects are exceeded (undertreatment, opioid tolerance), at rest, during procedures, or with anxiety	Treatment should be adjusted or changed based on the underlying cause
Procedural	Short duration, high intensity; occurs during minor and major procedures (dressing changes, wound debridement, rehabilitation)	- Minor procedures: Ketamine or propofol and distraction techniques - Major procedures: General or regional anesthesia, deep sedation Note: in case of anticipatory anxiety, anxiolytic therapy can be administered
Postoperative	Variable pain due to new and painful wounds in the process after surgical procedures; it usually lasts 2-5 days	Regional anesthesia, increase in opioid dosing, and awareness techniques
Chronic	Lasts for 6 months or longer after the wound has healed; neuropathic pain (burn-related nerve pain) is the most common and is described as a throbbing or constant burning sensation due to damage to nerve endings in the skin	Gabapentinoids as an adjunct to an opioid

α_2-Agonists: Dexmedetomidine and clonidine (weaker effects) are commonly used as adjunctive options to reduce opioid requirements. This group produces sedative and analgesic effects by stimulating α_2-receptors in the central nervous system. Dexmedetomidine is considered a first-line therapy for intubated burn patients and can be antagonized by using atipamezole; oral clonidine is used when weaning dexmedetomidine. A single administration of clonidine for analgesia in burn patients is not effective. α_2-Agonists can also be used for alcohol, nicotine, and opioid withdrawal; these are common scenarios in burn patients.[9,10,27]

Lidocaine: Intravenous infusion of lidocaine given to burn patients can decrease the pain score and morphine consumption; it is considered a reasonable second-line or third-line adjuvant agent in combination with PCA.[9,10,28]

Cannabinoids: This topic remains highly controversial, and there are few studies available due to legal and political regulations. Cannabis has been used for millennia to reduce pain; however, a recent study suggests that they most likely work on the emotional reaction to pain without reducing the pain score. Although in the United States the incidence of cannabis use is increasing among the burn patient population, more evidence is needed to support its indication for pain management.[10,29]

Gabapentanoids: Large injuries and intense pain experienced by burn patients can lead to neuropathic pain. Gabapentin and pregabalin act by facilitating gamma-aminobutyric acid neurotransmission and can be considered with a combination of opioids for treatment of postburn neuropathic pain or can be used in patients who are refractory to standard treatment. Gabapentanoids reduce pain scores and opioid consumption. In addition, pregabalin can reduce procedural pain, and gabapentin is useful in postburn pruritus. More studies are needed to determine their efficacy in nonneuropathic burn pain.[9,10,30]

Nonpharmacologic Treatment Options

To achieve a better result in relieving pain in burn patients, parallel therapy with nonpharmacologic treatment is recommended, especially during dressing changes. According to research conducted so far, 2 ways to help patients manage pain have been recognized: (1) distraction techniques and (2) awareness techniques, in which patients delve into the procedure that is being performed on them.

Distraction techniques

Avoidance interventions are designed to psychologically distract or distance the patient from the pain. The Multiple Resource Theory of Attention suggests that diverting attention toward a nonpainful stimulus may lessen the intensity of perceived pain.[31] There are multiple distraction techniques that can be used. In children, simpler techniques are used such as singing, listening to music, or reading a story. In adults, more laborious or more creative techniques are required, such as video games, virtual reality, or hypnotic analgesia.

Listening to music: Music has been for centuries a great ally of humans; music allows us to relax, disconnect, and distract ourselves, and it leads us to pleasurable emotions and joy. At present, it is useful for all of us and especially to doctors as a great tool to manage various aspects in the medical field. Music has been useful for the management of patients with acute and chronic pain from burns, which is generally accompanied by anxiety. It produces a much more harmonious and easy to handle environment for both the patient and the doctor. Listening to music may have a positive effect on patients' experiences of pain. Patients who underwent burn dressing changes while listening to music reported lesser pain scores compared with patients who did not listen to music. Therefore, music listening could be implemented as a routine activity whenever painful dressing procedures are anticipated.[32]

Virtual reality: Virtual reality (VR) visually isolates patients from the "real world." The helmet typically used to deliver VR blocks the patients' view of the hospital room and substitutes computer-generated images via small computer screens and lenses positioned near the patient's eyes. Noise-canceling earphones block or replace hospital noises with sound effects and relaxing background music from the virtual world.[33] In theory, while health care professionals are conducting invasive procedures, patients can, instead of cognitively remaining in the painful real world, perceptually escape into a pleasant, alternative 3-dimensional virtual world. In a controlled study of adult patients with an average of 21% of total body surface area burned, responses to range of motion exercises of injured extremities under an occupational therapist's direction were examined. Each patient spent 3 minutes of physical therapy with no distractions and 3 minutes of physical therapy in VR. All patients reported less pain when distracted by VR, and the magnitude of pain reduction by VR was statistically significant.[34] The efficacy of VR has been studied for decades, but a recent study went a step further. In addition to testing the efficacy in relieving pain and anxiety in pediatric patients during dressing change procedures, investigators demonstrated that there was an even greater difference in pain reduction between passive and active VR games.[35]

Hypnotic analgesia: Hypnotherapy is a medical practice that has been used for many years for pain management. Hypnotherapy is defined as a state of consciousness involving focused attention and reduced peripheral awareness characterized by an enhanced capacity for response to suggestion.[36] However, to achieve its effectiveness, patients must reach adequate levels of hypnosis that are reflected

in slow breathing and the patient's description of being in a safe place. The way to reach this optimal state is through the 5 stages in classical hypnosis: setting the stage, slowing of breathing and relaxation, suggestion for deepening of relaxation and hypnosis, suggestion for pain control, and alerting.[37,38] There are numerous studies that support its effectiveness. One study showed that, in a protocol of pain management in major burns, hypnosis reduced patient anxiety and reduced the need for early opioid delivery and decreased general anesthesia requirements, hospital length of stay, and costs.[39] Although the neural mechanism of hypnosis is not clear, recent neuroimaging studies have reported that it may be able to at least partially prevent painful stimuli from reaching neural regions associated with the perception of pain. With hypnotic induction, in painful conditions, there is less activation at the sensory cortex, precuneus, and cingulate gyrus, suggesting that the sensation of pain is dulled.[39,40]

Approach techniques

Approach techniques are based on making the patient aware of the procedure that is being performed. There are several; among them, the cognitive behavioral techniques stand out.

Cognitive behavioral techniques: Cognitive behavioral techniques have been used for many years and consist of the patient recognizing negative thoughts and behaviors and managing to modify them. The protocol is the assumption that maladaptive cognitions are causally linked to emotional distress; therefore, by modifying cognitions, emotional distress and maladaptive behaviors will decrease.[41] For treatment of burn patients, cognitive behavior techniques include diversion, information provision, coping skills, and relaxation techniques to modify the patient's thought process about the painful experience.[42] Cognitive behavior techniques in burn patients must be addressed in a way that they can differentiate the emotional part from the sensory part of the pain. This is achieved through the technique known as sensory focusing, which consists of reducing distress by distracting the individual from interpreting the meaning of the sensations, providing valuable self-regulatory information about the sensations, and by increasing perceptions of control.[43] A study showed that there is better pain management in burn patients who perform cognitive behavior techniques with sensory focus than in those who undergo distraction methods. In the context of ongoing medical management, sensory focusing increased ratings of pain relief and reduced patients' memories of pain during the procedure. There may be even greater pain relief after procedures, such as dressing changes, with cognitive behavior techniques.[44]

Complementary health: Several complementary techniques have been in use for many years in the medical field. Acupuncture is a technique practiced for more than 3000 years. Its effectiveness in pain management has been demonstrated, and there are numerous studies supporting its use for burn pain management.[45,46] Multiple endogenous substances are involved in acupuncture analgesia such as opiates (beta-endorphin, enkephalin, endomorphin, and dynorphin), 5-hydroxytryptamine, noradrenaline, dopamine, gamma-aminobutyric acid, acetylcholine, and orexin-A.[47] A controlled study conducted with 53 burn patients showed a great decrease in pain. Before acupuncture, the median pain score was 5, but, after treatment, median pain score was 1.5.[48] Experimental studies have shown the benefits of acupuncture during the acute phase of burns by decreasing pain and distress and subsequently improvement of wound healing, mainly due to the activation of angiogenic growth factors.[46,47] The fact that acupuncture has been maintained for centuries as a technique for pain management and that it continues to be used today is because it has demonstrated its great effectiveness. Massage therapy has also shown beneficial outcomes to mitigate pain during the rehabilitation phase of burn patients.[49]

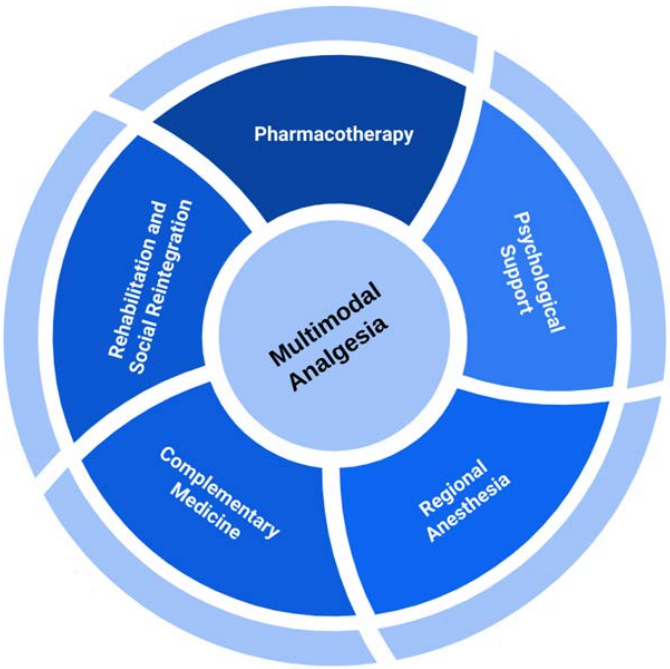
Pain, Stress, and Wound Healing

Several studies have described the influence of physiological factors in the modulation of the wound healing process. Studies in both humans and animals have revealed that psychological stress delays wound healing.[50,51] Angiogenesis is commonly used to evaluate the quality of wound repair due to its pivotal role in the wound-healing process.[52] Pain often leads to stress, and stress can affect wound healing; pain induces a series of neuroendocrine and immune changes that can alter wound healing, and stress induces a disruption of the neuroendocrine-immune equilibrium.[51] Most patients with impaired wound healing have multiple comorbidities, resulting in poorer outcomes, increasing the risk of infections, the length of hospital stay, and treatment costs. The association between pain and wound healing is well-documented, and its repercussions must be taken into consideration for the multimodal treatment plan of burn patients (Figure 1). In the long term, quality of life may be adversely affected.[50-53]

CONCLUSIONS

Burn pain management is challenging, occurs over a prolonged period of time, and requires multimodal and multidisciplinary strategies to achieve comprehensive management. It is important to consider the different phases of burn injury and pain, the need for frequent assessments of pain and anxiety levels during the day, and the inclusion of different activities in the design of an appropriate treatment plan.

FIGURE 1. The Multimodal Approach to Burn Pain Management



Creating standards of care is still challenging, and many studies on burn patients remain underpowered. Opioids are usually suggested as the first-line treatment for moderate to severe acute pain in patients with burns. In a multimodal approach, acetaminophen and nonsteroidal anti-inflammatory drugs are feasible options. Anxiety or posttraumatic stress disorder is common in burn patients; thus, treating these conditions is crucial. Severely burned patients may also undergo multiple painful procedures such as wound debridement, dressing changes, skin grafting, and physical therapy. Sensitivity to analgesics can fluctuate. Regular use of opioids is associated with tolerance, dependence, and abstinence; thus, nonpharmacologic adjuncts should be included before and after any procedure and throughout the treatment period. There is strong evidence showing positive results with music, VR, hypnosis, and psychotherapy. Neuropathic pain is common and also an important consideration in this population; gabapentinoids such as gabapentin and pregabalin are increasingly used since they have shown effectiveness in reducing neuropathic pain and pruritus in burn patients.

In general, pain management requires a comprehensive understanding of the complex physiology and dynamic pharmacokinetic changes occurring in the patient. Because high-level evidence-based standards of care are lacking, further studies are needed to improve and standardize pain management in burn patients.

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