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PAIN MANAGEMENT IN TRAUMA (MR HOFFMAN, SECTION EDITOR)

Pain Management in Burn Patients

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Abstract

Purpose of Review This review focuses on the characteristics of pain following burn injury, methods of assessment, multimodal pharmacological treatment, and non-pharmacological adjuncts.

Recent Findings Opioid medications are the cornerstone of burn pain management protocols. Given the current opioid epidemic, current research focuses on other analgesic, anxiolytic, and sedative medications including gabapentin, ketamine, and dexmedetomidine. Non-pharmacological interventions discussed include music, massage, and more recently virtual reality and hypnosis. Further study addresses psychosocial contributions to the pain experience and associated symptoms of anxiety, sleep disturbance, and pruritus.

Summary Optimization of burn pain management requires a holistic approach and development of protocols utilizing multimodal pharmacological therapy as well as adjunctive non-pharmacological therapies. Many barriers to improved pain control exist, including inadequate education and provider bias. There is a growing need for the incorporation of mental health professionals and pain management specialists into multidisciplinary care teams.

Keywords Burn injury · Pain management · Burn pain · Burns · Burn surgery · Multimodal therapy

Introduction

Survival rates following severe burn injury have increased substantially over the last 40 years secondary to improvements in resuscitation, wound care, critical care, and infection control. Prognosis is no longer limited to survival or physical functioning, but now extends to encompass quality of life measures including the capacity to live pain-free [1••]. Pain management is one of the most crucial and challenging aspects of modern burn care and necessitates appreciation for various treatment modalities (Table 1). When surveyed, over 50% of burn survivor group members reported ongoing burn-related pain beyond 10 years post-injury, consistent with findings of other studies [2, 3].

Failure to adequately control pain following burn injury has significant and long-lasting consequences [4, 5]. Uncontrolled pain has been associated with poor wound healing, diminished capacity to engage in rehabilitation, and longer hospital stays [6, 7]. In a study of recently discharged patients who had sustained large burns, Elsherbiny et al. found that 30% of patients could not bathe independently, 24% could not dress independently, and 34% described having extreme difficulty working in their old job [8]. Furthermore, they were affected in their capacity to be around family and friends, with 20% tormented by feelings of loneliness and 56% reporting feeling extremely sad.

Qualitative studies of burn patients' experiences describe "heart-snatching" and "splitting" pain that equated to psychologically scarring "catastrophe" and "torture" [9, 10]. The development of mood disorders, anxiety disorders, and posttraumatic stress disorder (PTSD) is unsurprisingly prevalent, as are issues with sleep disturbance, body image, and sexual intimacy [7, 11••, 12, 13]. In a longitudinal study of 128 survivors of major burns, pain severity at the time of discharge was found to be the sole consistent predictor of suicidal ideation at the time of follow-up, with greater pain severity representing enhanced risk [14].

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Table 1 Summary of pharmacological and non-pharmacological treatment modalities

Pharmacological	Non-pharmacological
Opioids	Initial medical management
Patient-controlled analgesia	Cooling
Intravenous continuous	Topical wound care
Intravenous bolus	
Oral	
Non-opioid	Supportive
Acetaminophen	Verbal acknowledgement of pain and suffering
Nonsteroidal anti-inflammatories	Spiritual care
Intravenous lidocaine	Psychotherapy
Topical lidocaine	
Gabapentinoids	
Antidepressants	Distraction
Selective serotonin reuptake inhibitors	Imagery
Serotonin-norepinephrine reuptake inhibitors	Jaw relaxation
Tricyclic antidepressants	Progressive muscle relaxation
	Relaxation breathing
	Music
Anxiolytics	Technological
Benzodiazepines	Virtual reality
Cannabinoids	Interactive gaming consoles
Sedatives	Physical intervention
Propofol	Massage
Ketamine	Aromatherapy
	Acupuncture
Alpha-adrenergic agonists	Other
Dexmedetomidine	Hypnosis
Clonidine	Laser therapy
	Transcranial direct current stimulation
	Extracorporeal shock wave therapy
Other	
Propranolol	
Nitrous oxide	

Despite evolving attitudes and available modalities, satisfactory amelioration of both acute and chronic burn-induced pain has proved difficult. Early studies advocated against polypharmacy, and data regarding non-pharmacological therapies were limited. Even with the current incorporation of multimodal pharmacotherapy and increasing utilization of non-pharmacological adjuncts, burn care teams struggle to meet patients' pain needs. Contributing factors may include lack of treatment protocols, practitioner fear of opioid side effects and addiction, and insufficient evaluation and underestimation of the scope of patients' symptoms [15••, 16, 17].

Pathophysiology of Pain After Burn Injury

Nociceptors within burned tissue are responsive to mechanical and chemical stimulation and are directly activated by heat [18••]. Temperatures high enough to cause necrosis stimulate release of inflammatory mediators resulting in immediate perception of pain. Thermal denaturing of proteins and loss of plasma membrane integrity contribute to cell death and leakage of mediators which trigger an intense inflammatory response (Fig. 1). Mediators involved in this local nociceptor sensitization and primary hyperalgesia include bradykinin, serotonin, histamine, eicosanoids, leukotrienes, platelet activating factor, interleukins, tumor necrosis factor (TNF), nerve growth factor, prostaglandins, thromboxane, adenosine, epithelial growth factor (EGF), basic fibroblast growth factor (bFGF), transforming growth factors, and platelet-derived growth factor [4].

Several ion channels have been implicated in the transmission of this signal, including TRPV1 (transient receptor potential vanilloid type 1 ion channel), TRPV2, and TRPV3. Noxious heat stimulates production of lipid metabolites 9-

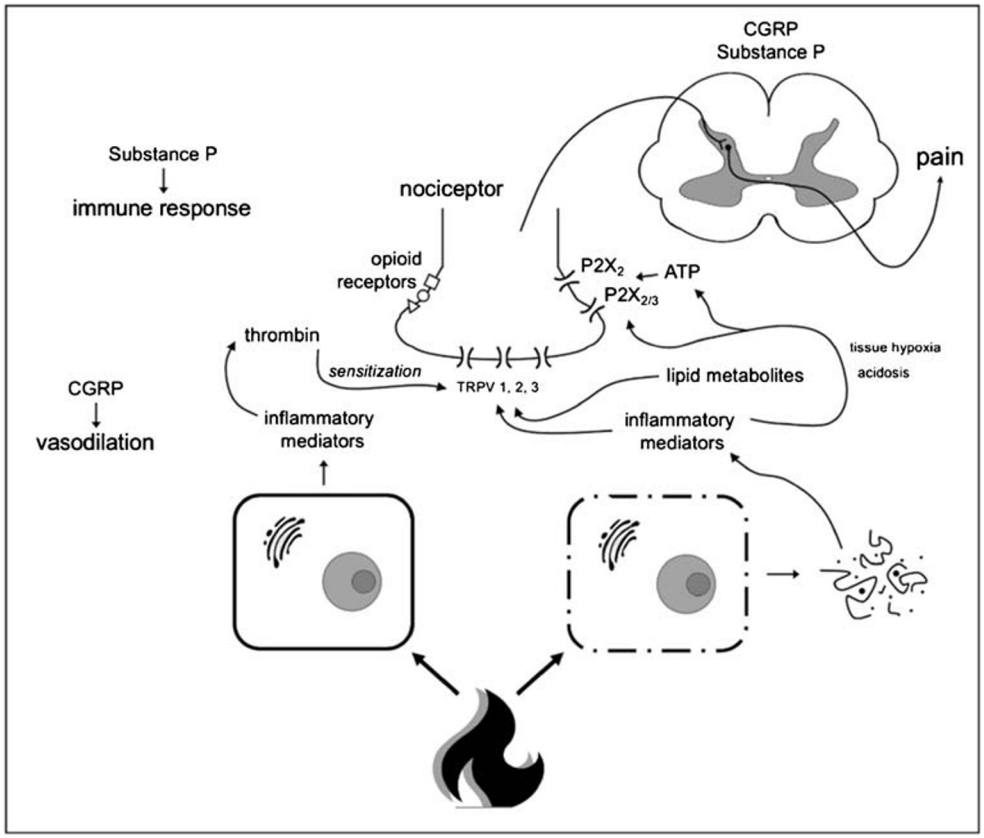

Fig. 1 Pathophysiology of pain from burn injury

and 13-hydroxyoctadecadienoic acids (9- and 13-HODE) which directly activate TRPV1, stimulating release of neuropeptides Substance P and calcitonin gene–related peptide (CGRP) from peripheral terminals of nociceptive primary sensory fibers. CGRP in turn induces vasodilation, while Substance P induces activation of the immune system.

Additionally, high concentrations of adenosine triphosphate (ATP) directly stimulate nociceptor ion channels including purinergic receptors $P2X_3$ and $P2X_3$. Tissue hypoxia and localized acidosis contribute to the immediate development of a pain response, with acid acting directly on TRPV1, TRPV4, $P2X_2/P2X_{2/3}$, and acid-sensing ion channels (ASIC). Production of thrombin by injury-induced activation of the coagulation cascade activates protease-activated receptors resulting in TRPV1 sensitization.

Endogenous modulation of pain by the neural system is primarily through opioid peptides including met-enkephalin, leukenphalin, b-endorphin, and dynorphin. These peptides then bind to μ (mu), δ (delta), and κ (kappa) receptors to achieve endogenous analgesia. Pain sensations are ultimately cumulatively transmitted via unmyelinated C-fibers and thinly myelinated Aδ-fibers to the dorsal horn of the spinal cord [3]. As a consequence of the processes contributing to primary hyperalgesia, secondary hyperalgesia ensues due to sensitization of a larger nociceptive field from continuous afferent firing by nociceptors in the surrounding tissue [19]. Although the total nerve density does not appear to significantly differ between scar and uninjured sites in patients with and without complaints of chronic post-burn pain, patients with chronic pain demonstrate significantly higher density of nociceptive nerve fibers in both scar sites and uninjured skin [20].

Associated Symptoms

Neuropathic Pain

Patients with both acute and chronic burn-associated pain also commonly exhibit components of neuropathic pain. This broadly encompasses all pain sensation caused by dysfunction or injury within the peripheral central nervous system [21]. It may not be accompanied by non-neuropathic chronic pain and frequently is associated with pruritus. Multiple mechanisms have been proposed. Severe burn injury results in the destruction of nerve endings thus temporarily rendering them insensate, but over time, the tissue may regenerate in a disorderly fashion [3]. Nerve compression and entrapment may also occur due to edema associated with the acute injury. Vascular occlusion of the vasa nervorum may also contribute. The resultant pain is typically described as a burning, stabbing, shooting, or electric sensation, like a “pins and needles”

sensation. Neuropathic pain must be approached as a distinct entity from other injury-associated pain and requires directed therapy.

Central Pain

Separate from the immediate impact of neuropathic pain is the idea of pathologic sensitization of the central nervous system from nociceptor input. While repeat exposure to noxious stimuli is intended to prompt protective hypersensitivity, in a normally activated system, this sensitivity returns to baseline after removal of the stimuli. Only discovered in the early 1980s, central sensitization has been identified as contributing to clinical pain hypersensitivity and has provided mechanistic explanations for why pain can sometimes outlast peripheral stimuli and extend beyond damaged regions of the body. Nerve injury can increase the potential for anatomic changes in nerve fibers that allow them to express neuropeptides that prompt central sensitization. *N*-methyl-D-aspartate (NMDA) receptors play a prominent role in the development of central sensitization, along with elevations in intracellular calcium that increase synaptic efficiency [22]. Additionally, genetic predisposition to central sensitization has been demonstrated [23]. Both of these findings offer opportunities for modulation of pain responses after burn injury, though more research is necessary on how burn injury specifically modulates central neuronal plasticity.

Psychogenic Pain

Pain is a complex sensory and emotional experience (Fig. 2). Functional magnetic resonance imaging (fMRI) studies of the brain show that over time, chronic pain becomes less closely associated with sensation, and more closely associated with arousal, emotion, cognition, and memory which alters the structure of the central nervous system [24]. The interplay of sensory and emotional experiences associated with pain contributes to sleep disturbance, exhaustion, depression, anxiety, and catastrophizing negative beliefs. Catastrophic thinking in relation to pain may heighten perceived levels of pain and emotional distress. Cognitive behavioral strategies for addressing negative thinking such as rumination, magnification-style and helplessness, mindfulness-based interventions, relaxation training, and sleep hygiene support the notion of pain resilience complementary to surgical and pharmacological interventions [25].

Sleep

Sleep disturbance in hospitalized burn patients is a major source of distress. The impact of inadequate sleep is often underappreciated and has significant implications on healing and time to recovery [26]. Both duration of rest and quality of sleep are affected by exogenous factors such as ambient light and noise, medical interventions, vital sign monitoring, and medication administration. Anxiety and depression, as well as pain, itch, and generalized discomfort, are also contributory. Prior to utilization of pharmacological sleep aids, sleep duration and quality should first be optimized with good sleep hygiene and minimization of caregiver disturbances.

Itch

Pruritus is one of the chief short- and long-term complaints of burn patients and has been found to cause significant distress and hindrance of functional recovery. An estimated 80% of burn patients will experience pruritus while hospitalized [27]. Ongoing symptoms can lead to skin breakdown and graft loss, potentially necessitating further grafting [28••]. For many, pruritus may persist for months to years after injury, with symptoms contributing to diminished quality of life.

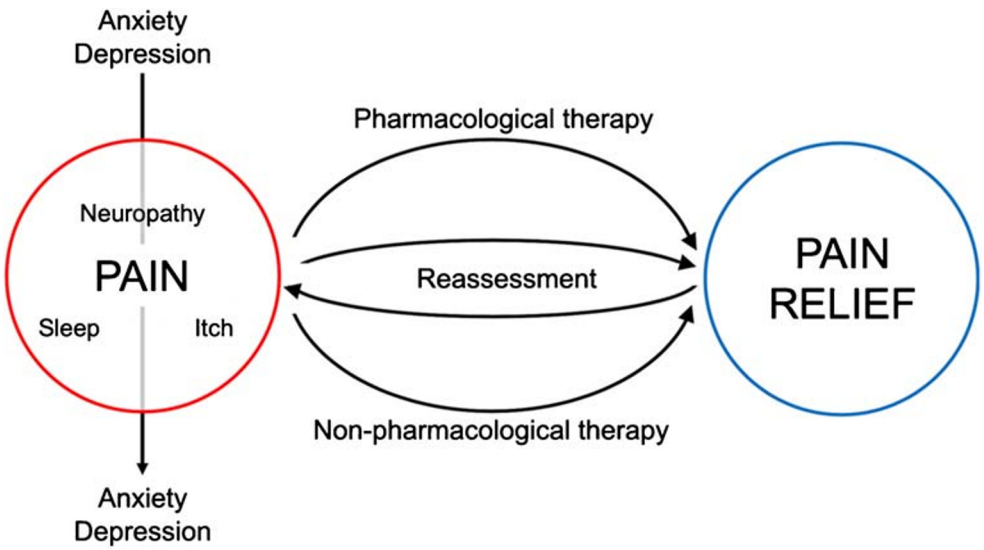

Fig. 2 Interplay of factors involved in pain control

Mild pruritus may be alleviated by topical applications including moisturizing lotions, antihistamine creams, and Preparation H, which contains the local anesthetic pramoxine. The use of topical tricyclic medications has been evaluated, but the efficacy is questionable [29]. For wounds that are well-healed, topical steroids can be considered. Oral antihistamines such as diphenhydramine or loratadine offer variable efficacy, as do cyproheptadine and hydroxyzine. Gabapentinoids demonstrate varying degrees of success [30, 31]. Non-pharmacological interventions such as massage, transcutaneous electrical nerve stimulation (TENS), pulse dye laser, and silicone gel sheeting have also been studied.

Assessment Tools

Adequacy of pain control is rooted in the ability to accurately discuss, measure, and document patients' symptoms in a standardized and easily reproducible fashion. In a 1998 publication on background pain, Jonsson et al. acknowledged having had no information regarding their patients' pain experiences prior to the development of their study [32]. Since that time, the conceptualization of pain as a fifth vital sign has raised recognition of the importance of frequent, regular measurement and documentation of pain levels [33–35].

A variety of validated scales and techniques have been employed. Visual analog scales (VAS) and basic numerical rating scales are common and are easy to use in most patient populations [19, 36]. It is important, however, that these scores are coupled with qualitative assessments of subjective self-reporting. Other frequently used tools include the McGill pain questionnaire and the Brief Pain Inventory (BPI). Tools specifically measuring anxiety such as the State-Trait Anxiety Inventory (STAI) and the Burn Specific Pain Anxiety Scale (BSPAS) can be used in addition to provide more holistic assessments [37]. Alternative measurements may prove more useful in pediatric patients. In all cases, data may be challenging to interpret as they are highly subjective and inconsistently correlate with objective signs and indicators of pain including vital signs [38]. Ultimately, easily repeatable and repeatedly collected measures of a patient's pain and their response to interventions aimed at addressing that pain is critical for helping patients return to a functional level of comfort.

Additional screening and assessments are needed when considering associated psychiatric measures. Screening tools focused on psychometric measures include Patient Health Questionnaire (PHQ-9), Columbia Suicide Severity Rating Scale Triage Indicators (CSSRS-Assessment), Generalized Anxiety Disorder 7-Item Scale (GAD-7), Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5), Pain Catastrophizing Scale (PCS), and the Patient Reported Outcomes Measurement Information System (PROMIS) pain measure. These are brief and narrow in scope and provide an indication for further evaluation and potential treatment interventions.

Pharmacological Therapy

Opioids

Given the central role that the opioidergic system plays in pain perception, opioid medications are typically the cornerstone of burn pain management [3, 16, 39•]. These agents act primarily on μ receptors in endogenous pain pathways. Multimodal approaches capitalize on the synergistic effects of different drug classes which achieve analgesia via pathways affecting pain perception and modulation [40]. With the widespread adoption of early recovery after surgery (ERAS) protocols and the curtailing of prescribing patterns amidst the opioid epidemic, current pain management protocols increasingly rely on non-opioid analgesics as well as anxiolytic and sedative agents [7, 41, 42].

Specific drug choice is influenced by the type of pain being managed and overall clinical condition of the patient (Table 2). Patient-controlled anesthesia (PCA) is beneficial for intubated patients or those who otherwise require continuous narcotic administration for the treatment of background pain [18••]. Intrathecal administration of morphine for this purpose has also been described [43]. Background pain is otherwise best managed with oral narcotics, taking advantage of longer durations of action, while transient procedural pain is best alleviated with high-potency short-acting intravenous agents. PCA bolus administrations also prove valuable for the control of intermittent breakthrough and procedural pain and have the added benefit of giving patients a sense of participation and control of their pain management.

Short- and long-term side effects of opioid use include constipation, respiratory depression, sedation, pruritus, sleep cycle interference, nausea, and vomiting. Many of these effects are dose-dependent, and risks can therefore be mitigated by frequent assessment and dose adjustments [3, 7, 18••]. Even short-term use places patients at risk for physical and psychological dependence which then plays into risk for addiction and abuse [35]. Over time, opioid medications can degrade and destroy μ receptors causing dysregulation of the body's pain sensory system and potentially facilitating the transition from acute to chronic pain. The long-term efficacy of opioid therapy for chronic pain is controversial.

With prolonged use, patients may also develop tolerance leading to ongoing dose escalation. While tolerance may build up slowly over a prolonged hospital course, it is also possible to develop tolerance rapidly within a perioperative time frame. Patients with a history of chronic opioid use pre-injury are more likely to demonstrate tolerance; however, the effect can be observed in opioid-naïve patients as well. Recent

Table 2 Example protocol for multimodal therapy protocol by clinical setting

Therapy	Initial dose considerations	ICU	Wards	Clinic	Home
Intravenous lidocaine	1.5 mg/kg loading dose 1–2 mg/kg/h	X			
Intravenous ketamine	0.1–0.5 mg/kg loading dose 0.05–0.4 mg/kg/h	X			
Dexmedetomidine	0.2–0.7 μg/kg/h	X			
Propofol	5 μg/kg/min initial dose titrate by 5–10 μg/kg/min	X			
Opioid PCA continuous	Per unit protocol	X			
Opioid PCA bolus	Per unit protocol	X	X		
Opioid intravenous bolus	Timed for procedures (dressing changes, shower, rehabilitation/therapy)	X	X		
Benzodiazepines	Procedural	X	X	(X)	
Opioid oral	Transition from IV as soon as feasible		X	X	X*
Acetaminophen	325–650 mg q4–6h Not to exceed 4 g/d	X	X	X	X
NSAIDs		X	X	X	X
Gabapentin	100–300 mg TID initial dose (dependent on renal function) Maximum dose 3600 mg/d	X	X	X	X
Antidepressants		X	X	X	X

*With the plan to reduce utilization to zero once open wounds have closed

studies have aimed at evaluation of methadone as a strategy to mitigate opioid tolerance and reduction of central sensitization. Its long half-life lends to effective treatment of chronic background pain in addition to coverage of acute pain [18••]. Chronic use of opioid medications may also result in opioid hyperalgesia with loss of analgesic efficacy and enhanced pain and sensitivity [44]. The involved mechanism is not well-understood but may be in part secondary to the interaction of opioids with immune cells via toll-like receptors. Developing hyperalgesia may go unnoticed or underappreciated if effects are attributed to presumed development of tolerance. While the tolerance effect can be overcome by escalating opioid dosing, increasing opioid doses in the setting of opioid-induced hyperalgesia will worsen symptoms. Opioid-induced hyperalgesia is best combatted through down-titration of opioid agents, rotation of drugs used over time and utilization of non-narcotic medications.

Non-opioids

NSAIDs and Acetaminophen

Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs) are valuable non-opioid adjuncts given their antipyretic, anti-inflammatory, and analgesic effects [45••]. They can act synergistically with opioids, and may reduce opioid requirements by 20–30% [3]. Historically, there has been a relative avoidance of NSAID use for burn-induced pain given concerns for gastrointestinal and renal side effects as well as diminished platelet activity. While these risks may outweigh the benefits in critically ill burn patients, NSAIDs should be considered a viable option in smaller burns.

Lidocaine

Interest in adjunctive use of intravenous lidocaine has grown; however, data are limited [46]. In a recent randomized controlled trial, Abdelrahman et al. concluded that intravenous lidocaine was safe and reduced opioid requirements by 25% [47]. These findings are in contrast to the earlier work by Wasiak et al. which noted no difference in opioid requirements with the adjunctive lidocaine use [48].

Gabapentinoids

Gabapentin and other gabapentinoids such as pregabalin selectively affect the nociceptive process involving central sensitization. Resultant analgesia is most pronounced in the treatment of neuropathic pain, and there is also some evidence in support of an opioid-sparing effect [31, 49, 50]. Gabapentinoids have also been demonstrated efficacy in treatment of pruritus [30]. When gabapentin was compared to ketamine, dexmedetomidine, and nitrous oxide for adjunctive therapy with opioids, Chaghazardi et al. favored the use of gabapentin as it is cheaper and is administered orally [51].

Antidepressants and Anxiolytics

Antidepressant agents such as tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin-norepinephrine reuptake inhibitors (SNRIs) have proven to be valuable adjuncts in multimodal pain management strategies. In low doses, amitriptyline, a TCA, may help with neuropathic pain by activating descending spinal cord inhibitory pathways. Additional benefit is gained through the concurrent action against concurrent anxiety, depression, and insomnia. Duloxetine may additionally provide benefit in increasing inhibitory inputs and addressing central sensitization. Benzodiazepines are frequently added to pain regimens for additional anxiolysis. Cannabinoid usage has also been described but is lacking in supportive evidence [45••].

Ketamine

In 1978, Demling et al. explored the use of ketamine to aid in tangential excision of burn eschar, finding it to be an effective and safe anesthetic option [52•]. Benefits include diminished respiratory depression and relative preservation of hemodynamics, though acute increases in blood pressure and heart rate can be observed [45••]. The known side effects include nausea, vomiting, increased airway secretions, hallucinations, mood alterations, bizarre dreams, and emergence delirium.

While generally utilized for its capacity to induce a state of dissociative anesthesia, interest in the use of ketamine for analgesia has been increasing. A systematic review identified only four heterogeneous trials, and the authors concluded that it was impossible to pool results or perform a meta-analysis [53]. It was felt, however, that some analgesic efficacy had been demonstrated particularly regarding the capacity to reduce secondary hyperalgesia through inhibition of NMDA receptors when compared to opioid therapy alone [28••]. Given the role of the NMDA receptor in perpetuating central sensitization, ketamine may prove useful in the management of chronic pain after burn injury [22].

Alpha-Adrenergic Agonists

Dexmedetomidine functions primarily as a sympatholytic. It has become a popular agent in the management of intubated patients given its sedative, anxiolytic, and analgesic properties [54]. The known side effects include bradycardia and hypotension, particularly with higher dose infusions. Its prime benefit is the minimal associated risk of respiratory depression. While clonidine is most commonly utilized as an anti-hypertensive, like dexmedetomidine, it possesses sedative effects. Dexmedetomidine has a shorter duration of action and is more selective for α-2 receptors than clonidine.

Propranolol

As prior studies have noted that activation of β-adrenergic receptors may augment pain sensation, it has been suggested that antagonists such as propranolol could be effective in reducing pain after burn injury. While there are data regarding propranolol administration to blunt the hypermetabolic response to burns, there is currently no evidence supporting an analgesic effect [55].

Nitrous Oxide (Enotox)

Nitrous oxide has been shown to achieve an analgesic effect via release of endogenous opioids. Benefits include fast onset and minimal associated side effects; however, the need for face mask administration may limit more widespread utilization [16].

Considerations for the Use of Pharmacological Management

The use of a variety of the standard formulations of pharmacological pain therapy needs to be considered specifically in the setting of thermal injury and scar formation. Topical preparations of analgesics may not be safe early in the healing process due to absorption from open wounds, whereas once the wound has closed penetration of those medications into scar tissue may be highly variable. Disruption of central sensitization with regional anesthesia may be an opportunity for future investigation, but without addressing ongoing stimulus from injured nerves caught in scar, many questions are left to be answered.

Non-pharmacological Therapy

Pain perception is complex and involves physical stimuli as well as context, cognition, and mood [33]. Non-pharmacological interventions in particular may alleviate many of the non-physical components affecting pain perception. It may be easy to underestimate the value of basic physical and psychosocial interventions. In the acute post-injury state, the importance of cooling and initial wound management with application of topical medications and dressings cannot be understated [28••, 45••, 56, 57]. Verbal acknowledgement of patients' pain and suffering from providers is crucial in both acute and chronic settings. Overall patient experience and satisfaction with pain control can be aided by additional supportive measures such as providing religious and spiritual care to desiring patients [58].

Several interventions aimed at reduction of pain severity have been investigated [59]. Impact on anxiety has also been examined, although in most studies, this is a secondary end-

point after the consideration of pain [60]. In a recent survey of the American Burn Association (ABA) members, Voss et al. described varying practice patterns utilized during outpatient dressing changes [61]. Most were pre-medicated with oxycodone and other oral opioids. While practitioner perception of the efficacy of non-pharmacological interventions was variable, 68% employed at least one adjunct. The majority represented distraction techniques, with music, movies, and television most common.

There are a number of evidence-based treatments available including cognitive behavioral therapy (CBT), mindfulness-based interventions, Acceptance and commitment therapy (ACT), emotional awareness and expression therapy (EAET), and biofeedback training. Basic distraction techniques, which impact modulation, are often highly effective and can be quickly implemented, requiring minimal guidance. Pathophysiology of this effect is felt to be related to gate control, whereby dorsal root nociceptors are inhibited by suppression of painful output by non-noxious stimuli [62]. Distraction allows for decreased attention to pain perception, reduced time spent thinking about the pain sensation, and subsequent diminished perception of pain. This approach can be adapted for patients of all ages. In children, distraction interventions may be as simple as blowing bubbles or counting. Other simple techniques employed in the adult population include deep breathing, progressive muscle relaxation, and jaw relaxation. Imagery-based distraction provides infinite options with details tailored to the individual and circumstances.

Music

Music is frequently employed as an easily implementable, portable, and customizable form of distraction, effective in mitigating pain and anxiety [45••, 63]. The effect is achieved by increased endorphin secretion as well as a gate control mechanism in which cerebral cortical and thalamic inhibitory impulses block sensory fibers at the spinal cord from transmitting pain information to the brain.

While music has been shown to be independently beneficial, it appears to be most efficacious when utilized alongside pharmacological therapy and other non-pharmacological adjuncts. In a small, randomized trial, Hsu et al. demonstrated a significant decrease in reported pain before, during, and after dressing changes performed with music, although no difference in morphine dosing was demonstrated between the experimental and control groups [64]. Similarly, Zhang et al. found significantly improved pain control in patients receiving both tramadol and self-selected music during outpatient burn dressing changes when compared to patients receiving tramadol alone, music alone, or controls [65].

Massage, Aromatherapy, and Acupuncture

There is some thought that massage therapy derives efficacy via gate control, but there is evidence that massage provides analgesia through an oxytocin response and possibly via serotonergic and dopaminergic pathways [62]. As with music, massage has been demonstrated to provide relief alone or as a component of a multimodal pain management protocol. Massage as a sole adjunct may potentially improve pain, anxiety, and itching [66, 67]. The efficacy of massage on chronic pain associated with burn scars has been studied, though without insight into potential to reduce analgesic consumption [45••]. Work by Ghezeljeh and colleagues has shown a significant improvement in both pain control and anticipatory anxiety with a combination of music and massage, as compared to either intervention alone or controls [67, 68].

Aromatherapy as an adjunctive pain control method may offer some benefit, but is likely more useful in the setting of massage therapy [69]. Overall, there is a lack of convincing evidence for independent usage. Acupuncture therapy has been studied as a strategy to reduce peripheral hyperalgesia, but appears to provide relief in only a subset of patients [45••]. Additional modalities that have been described include extracorporeal shock wave therapy, non-contact low-frequency ultrasound, transcranial direct current stimulation, and whole body vibration.

Virtual Reality, Interactive Gaming Consoles, and Hypnosis

A systematic review and meta-analysis by Scheffler et al. found that techniques based in virtual reality or hypnosis were the most effective non-pharmacological interventions for procedural pain [70]. The immersive experience of virtual reality technology provides a powerful form of distraction. The majority of current studies demonstrate at least a modest improvement in pain with application of virtual reality–based interventions, particularly in the setting of dressing changes and other procedural interventions [71–74]. Evidence regarding impact on anxiety is more equivocal.

While some groups have utilized commercially available virtual reality technology, there has been some success in developing and utilizing more cost-effective adaptations to achieve similar pain reduction [75, 76]. The use of interactive gaming consoles has achieved similar effects. A pilot trial performed during burn rehabilitation demonstrated reduced pain with gaming console use, with a pronounced effect in patients with higher baseline pain levels [77]. As with virtual reality–based strategies, benefit may stem from increased levels of dopamine release as well as cognitive distraction [45••].

The adjunctive use of hypnotic techniques has grown in popularity and has been increasingly examined in recent

literature, with findings suggestive of significant improvement in both pain and anxiety [78–80]. Dissociation allows patients to detach from painful stimuli by engaging in an altered state of consciousness through increased receptivity to suggestion. The primary limiting factor to more widespread adoption is the need for administration by a trained clinician.

Lasers

Laser therapy for burns and associated scarring has gained a great deal of traction over the past 10 years, with most recent practices primarily relying on carbon monoxide fractional ablative lasers. Pain and inflammation associated with burn wound healing may be improved with laser therapy through inhibition of the release of cyclooxygenase-2 and prostaglandins as well as through inhibition of nerve fiber transmission [81]. The majority of the current literature is focused on the efficacy of laser therapy on hypertrophic scarring. Although data regarding the impact specifically on burn pain remain scarce, preliminary studies appear promising [82]. One randomized controlled trial reported significant decrease in scar pain after 6 weeks of treatment, with effects lasting for at least an additional 6 weeks post-treatment [45••]. Other studies noted improvement in pain, pruritus, and vascularity following therapy, with best effects achieved in scars less than 6 months old.

Special Populations

Burn Pain in Children

Burn injuries sustained during childhood are traumatizing to patients and families alike and require concurrent management of pain and associated psychosocial factors [83•]. Parental presence and separation contribute the stress of the painful experience depending upon the child and the circumstances [28••, 84]. Inadequate management of acute pain has been shown to have significant long-term implications in this population. A recent work by Nelson et al. looking at the Burn Model System National Database demonstrated that pediatric patients' perceptions of the impact of pain on their lives was associated both cross-sectionally and longitudinally with decreased physical functioning, depressive symptoms, and challenges with peer relationships [85]. Animal studies suggest that pain experiences early in life can sensitize excitatory pain pathways, with associated downstream consequences [86].

One of the most significant barriers to achieving adequate pain control in the pediatric population is the ability to gauge a child's pain level at a given time. This proves particularly challenging in younger children who are pre-verbal [28••]. A number of tools have been proposed and evaluated and have varying applicability depending on the patient's age. Observation-based scales such as the Pain Observation Scale for Young Children (POCIS), the COMFORT-B scale, the Observational Pain Assessment Scale (OPAS), the FLACC scale, and the Children's Hospital of Eastern Ohio pain scale (CHEOPS) have higher utility in infants and toddlers, as opposed to visual analog scales (VAS) which prove less reliable in this setting [87]. The choice of tool may be based on a balance of reliability and ease and speed of use. CHEOPS remains a viable option for assessing preschoolers, in addition to the Wong-Baker FACES Pain Rating Scale and others. Pediatric pain questionnaires become useful in school-age children in addition to visual analog and FACES scales. Adolescents can generally be assessed within the same framework as adults.

While baseline pain has been shown to be manageable, acute and procedural pain generally proves more challenging. As with adults, most protocols rely on appropriately dosed and monitored pharmacologic therapy with opioids and non-opioid adjuncts. The use of agents such as ketamine and benzodiazepines also addresses anxiety and fear components [84]. Various non-pharmacological strategies have proven successful. In addition to medical play facilitated by child life specialists, technology-based modalities for distraction from procedural pain have increasingly gained traction [88, 89]. Tablet use, as well as virtual reality and multimodal distraction devices, has been demonstrated to improve both pain and anxiety when used in combination with standard pharmacological therapy [90–92].

Burn Pain in Pregnancy

Literature regarding burns during pregnancy is relatively scarce and provides minimal guidance regarding pain management in these patients. The incidence of concurrent pregnancy and burns has been cited at 3–7%, with the majority of the injuries being small and occurring secondary to accidents in the home [93]. With larger burns, pain management is highly complex given the need to minimize teratogenic risk and avoid NSAIDs due to the risk of premature closure of the ductus arteriosus [94]. In a recent case report, Roy et al. describe utilization of ketamine as a component of a multimodal approach to pain in a patient in her third trimester of pregnancy. The authors advocate for a multidisciplinary approach for management of these patients.

Burn Pain in the Elderly

The incidence of elderly patients sustaining burns is increasing as the average age of the population grows [95]. Care of these patients is impacted by altered metabolism, immunosuppression, malnutrition, increased comorbidity rates, and associated higher rates of polypharmacy [96]. Management may be complicated by cognitive impairment or difficulty with

communication which may limit the utility of many pain assessment tools and scales. Concern for oversedation and generalized lack of comfort in managing pain in this population contribute to the tendency of providers to undertreat pain in the elderly [28••]. The additional input from consultants in Geriatric Medicine can be invaluable in providing a balanced approach to this special population.

Conclusions

Updated ABA guidelines on pain management, due for publication in 2021, are expected to reflect significant strides in the understanding of burn-related pain over the last decade [97]. Approaches and attitudes toward pain management have evolved significantly, and great strides have been made in the pursuit of non-pharmacological adjuncts. The development of multimodal pharmacologic protocols has somewhat reduced dependency on opioid therapy; however, provider bias stemming from inadequate education continues to be a barrier to optimized pain management. Implementation and expansion of training programs for newly appointed and established providers may address gaps in knowledge and the impact of pre-existing attitudes toward various pain management modalities [40].

More emphasis must be placed on the importance of knowledge sharing and patient preparation for procedures [41]. In a qualitative study of burn patients' experiences with pain management, Li et al. noted that many felt inadequately informed regarding burn pain management, medical information relating to pain, and details about analgesics and their effects [10]. Patients also reported that their pain was not assessed with adequate frequency and that they felt they were not taken seriously enough regarding the severity of their pain.

Further integration of pain specialists, mental health professionals, and palliative care specialists into care teams is needed in order to augment already highly multidisciplinary approaches [40]. This necessity is a chief concern when facing both medical and ethical challenges of end-of-life care. The landmark 1997 US Supreme Court ruling in *Vacco v. Quill* highlighted patients' rights to treatment of pain with aggressive measures. Furthermore, a recent systematic review of palliative care literature notes that most research has focused on interventions for physical symptoms without adequately addressing other important domains for quality of life [1••]. Additional attention to patients' processes of normal adaptation is needed in order to fully address pain and suffering [98]. Given the profound psychological consequences of burn injury and the associated pain experience, improved focus on the holistic care of the patient is needed.

Compliance with Ethical Standards

Conflict of Interest The authors declare they have no conflicts of interest with the contents of this article.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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