

## Pain Management

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### Introduction

Controlling pain presents a challenge from initial emergency room care through the rehabilitation phase of care. Burn pain is very likely the most difficult form of acute pain to treat from any type of etiology. Not only is the type of tissue damage with a burn injury likely to generate unusually high levels of pain, the nature of standard burn care is likely to worsen whatever pain is present. Wound care and therapies can generate pain that is equivalent or exceeds that experienced by the patient at the time of the injury. Pain, in addition to being a source of outright suffering in patients, can interfere with wound care and therapies as well as lengthen hospitalization. Moreover, the amount of pain experienced by hospitalized children and adults with burn injuries appears associated with long-term post-traumatic stress and general emotional distress. As such, there are practical as well as humanitarian reasons to control burn pain aggressively.

In terms of treatment, pain during hospitalization can be classified as background (that which is present while the patient is at rest; pain of lower intensity and longer duration), procedural (more intense, short-lived pain generated by wound care or therapies), breakthrough (spiking of pain levels that occur when current analgesic efforts are exceeded), and post-operative. Chronic pain is that which lasts longer than six months; this type can be a challenge for outpatient therapy. Most burn pain results from tissue damage. However, it is important to be aware that pain from nerve damage may be present, particularly in patients with amputations or limb evulsions. Pain from nerve damage is often treated differently than conventional burn pain.

Because burn pain is highly variable and cannot be reliably predicted by clinical assessment of the patient or their burn wound, we recommend a structured approach to burn analgesia that incorporates both drugs and alternative therapies, targets specific pain issues unique to the burn patient, and can be tailored to expected variations in patient need and institutional capability. In describing this treatment approach, it is important to emphasize that we borrowed heavily from a chapter by Patterson & Sharar in Bonica's text, The Management of Pain (Loeser, 2001). One clear goal is to avoid the undertreatment of burn pain, an unfortunate reality in the settings of adult and pediatric burn care, and more historically described for other acute pain settings. Perry et al noted that burn staff members failed to medicate patients adequately with opioids, despite education regarding the low risks for addictive and other side effects. These investigators offered a theory on this issue, proposing that staff members required to perform repeated and painful procedures on these patients had a need for patients to demonstrate pain as a means to create a psychological distance between the themselves and the realities of burn care. Alternatively, the fear of creating dependence on opioids may explain the reluctance of some burn care staff to aggressively treat burn pain. However, there is currently no evidence that opioid addiction occurs more commonly in burn patients than in other populations requiring opioids for acute pain (~1/3000).

In the generalized burn pain management model, selection of an analgesic regimen is individualized and based upon two broad categories: 1) the clinical need for analgesia (i.e., treatment of background vs. procedural vs. postoperative pain), and 2) limitations imposed by the patient (presence of intravenous [IV] access, endotracheal tube, or opioid tolerance) or by clinical facilities (available monitoring capabilities and personnel). The presence or absence of IV access directly influences analgesic drug choice, particularly in children in whom IV access may be problematic. Patients who are endotracheally intubated and ventilated are "protected" from the risk of opioid-induced respiratory depression; thus, opioids may be more generously administered in these individuals, as is often indicated for complex burn debridement procedures in patients with more extensive or severe burn injuries. Individual differences in opioid efficacy should be considered in all patients, including opioid tolerance in patients requiring prolonged opioid analgesic therapy or in those with preexisting substance abuse

histories. Due to the development of drug tolerance with prolonged medical use (> 2 weeks) or recreational abuse of opioids (both commonly seen in burn patients), opioid analgesic doses needed for burn analgesia may significantly exceed those recommended in standard dosing guidelines. One clinically relevant consequence of drug tolerance is the potential for opioid withdrawal to occur during inpatient burn treatment. Thus, the period of inpatient burn care is not an appropriate time to institute deliberate opioid withdrawal in the substance-abusing patient, because such treatment ignores the very real analgesic needs (background pain and wound care pain) of these patients. Similarly, when reductions in analgesic therapy are considered as burn wounds heal, reductions should occur by careful taper, in order to prevent acute opioid withdrawal syndrome.

Institutional capability to provide adequate monitoring (pulse oximetry, independent patient observer) as required for "conscious sedation" may also dictate which agents are used for procedural analgesia, as some of the more potent opioids (e.g., fentanyl) and agents like ketamine may provide levels of sedation beyond that of mere analgesia. Obviously this distinction between analgesia and conscious sedation is subjective, and requires both individual and institutional interpretation to assure safety and practicality in meeting proposed monitoring guidelines for conscious sedation. The use of potent opioids and anxiolytics should only occur in settings with adequate monitoring, personnel, and resuscitation equipment appropriate for the degree of sedation anticipated. For most wound debridement procedures opioid analgesia with minimal sedation is sufficient, and no special monitoring is required. Larger or more potent doses of opioids, or the concurrent use of anxiolytic sedatives (e.g., benzodiazepines) may produce more pronounced sedation ("deep sedation") where patient-staff communication and/or consciousness are lost. Current guidelines of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), as well as physician specialty professional organizations, dictate both general and specific levels of monitoring (e.g., continuous pulse oximetry, presence of an independent observer specifically responsible for monitoring ventilation and vital signs) for patients requiring this level of analgesia/sedation.

Tissue damage at the burn site is the predominant mechanism of pain and suffering in these patients acutely, pharmacologic treatment with potent opioids, anxiolytics, and other agents (e.g., ketamine) is the first line of therapy. Our bias is that nonpharmacologic methods of treating burn pain are also extremely useful; although some nonpharmacologic pain control techniques should be second nature to the staff and integrated into standard care (e.g., minimizing the number and intrusiveness of dressing changes, limb elevation, brief educational approaches). Others are more practically implemented after a stable pharmacologic regimen is established (e.g., hypnosis). To reinforce a consistent approach to analgesic management, particularly in centers where house staff physicians and/or nursing staff may rotate or change frequently, the establishment of detailed guidelines may help physicians and nurses with choosing and administering analgesics that target specific analgesic needs, as shown in Figure 1. To maximize simplicity and utility, it is recommended that such guidelines be safe and effective over a broad range of ages, be explicit in their dosing recommendations, have a limited formulary to maximize staff familiarity, and allow the bedside nurse to continuously evaluate efficacy and safety. In addition, the regular use of a weight-based pediatric medication worksheet (placed at the bedside and in the patient record), containing all analgesic and resuscitation drugs likely to be administered, provides a supplemental safeguard against accidental overdose, particularly in the young pediatric age group.

## **Pharmacologic Approaches**

Our description of pharmacologic approaches to burn pain is again dependant on the Patterson & Sharar chapter in Loeser et al (Loeser, 2001). In describing pharmacologic approaches for burn analgesia, three consistent observations can be made. First, for patients with injuries extensive enough to require hospitalization, pain from the burn itself is severe. Thus, potent opioids form the cornerstones of pharmacologic pain control in these patients, leaving few indications for the mild to moderate analgesia provided by non-steroidal anti-inflammatory (NSAIDs) or acetaminophen as sole therapies, with notable exceptions of the rehabilitative phase of care and outpatient treatment. However, these less potent analgesics are still of value when combined with opioid analgesics, as the small but measurable analgesia they provide lessens the dose requirements for accompanying opioids (i.e., opioid-sparing effect). Second, because burn pain has well-defined components -- background, procedural, breakthrough, and postoperative pain -- pharmacologic choices for analgesia should target each pain pattern individually. Finally, because burn pain will vary somewhat unpredictably throughout hospitalization due to surgical intervention, activity levels, etc., analgesic regimens should be continuously evaluated and reassessed to avoid problems of under- or over-medication. A reliance upon nurse assessment of patients' burn pain can be problematic, however, as it is well documented that nurses' and patients' assessment

of burn pain and analgesia are not always comparable, with nursing staff typically underestimating the need for analgesic therapy.

### **Opioids**

Opioid agonists are the most commonly used analgesics in the treatment of burn pain, in part because i) they are potent, ii) the benefits and risks of their use are familiar to the majority of care providers, and iii) they provide some dose-dependent degree of sedation that can be advantageous to both burn patients and staff, particularly during burn wound care procedures. The wide spectrum of opioids available for clinical use provides dosing flexibility (i.e., variable routes of administration, variable duration of action) that is ideal for the targeted treatment of burn pain. The chemical properties of opioids in burn patients are not consistently different from non-burn patients, although decreased volume of distribution and clearance, and increased elimination half-life have been reported for morphine. Similarly, potency of opioids has inconsistently been reported as increased and decreased in burn patients.

The route of opioid administration is an important issue in burn patients, with the principal choice between IV or oral administration dictated by the severity of burn (critically ill patients require IV access and may have abnormal gut function) and the high risk of burn patients for developing intravascular catheter-related sepsis; hence, physician reluctance to maintain long-term IV access. Intramuscular opioid administration is avoided because of the need for repeated, painful injections, and because of variable vascular absorption due to unpredictable compartmental fluid shifts and muscle perfusion in burn patients, particularly those undergoing acute, burn shock resuscitation. Patient-controlled analgesia (PCA) with IV opioids offers the burn patient a safe and efficient method of achieving more flexible analgesia. PCA also offers the patient some degree of control over his/her medical care, this often being a major issue for adolescent and young adult burn patients, and those whose waking hours are often completely scheduled with care activities ranging from wound care to physical and rehabilitation therapy. Some studies comparing PCA opioid use to other routes of administration in the burn population have shown positive, but limited benefits of PCA, although others have shown that patients may prefer an attentive nurse and that the cost of this technology when used with burn patients may not be justified. The PCA administration of potent, short-acting opioids (e.g., alfentanil, remifentanil) for procedural analgesia may also have a useful role in burn analgesic management, but is yet to be investigated. Finally, oral transmucosal administration of opioids is reported in burn patients, and appears to be particularly advantageous in those patients without IV access and in children.

### **Non-opioids**

The list of non-opioid analgesics in widespread use for the treatment of burn pain is currently limited, although not without potential benefit. Oral NSAIDs and acetaminophen, as outlined above, are only mild analgesics that exhibit a ceiling effect in their dose-response relationship, rendering them unsuitable for the treatment of typical, severe burn pain. However, they are of benefit in treating minor burns, particularly in the outpatient setting. Topical application of NSAIDs on burn wounds can theoretically inhibit pain signals at the injury site with minimal systemic uptake, yet does not result in significant analgesia. The opioid agonist-antagonist drugs (e.g., nalbuphine, butorphanol) produce "mixed" actions at the opiate receptor level, theoretically providing analgesia (agonist property) with lesser side effects (antagonist properties), but also exhibit ceiling effects. Although studies have shown this class of drugs to be effective in treating burn pain, experience with them is both limited and suggestive of efficacy in patients with only relatively mild burn pain.

Antidepressants, anticonvulsants, and clonidine have been proposed as potential analgesic agents for burn pain based on their known mechanisms of action in other pain states (e.g., neuropathic pain), yet have not been studied in the setting of burns. As neuropathic pain can occur in patients with healed burns, these agents may have specific application in this fortunately uncommon setting.

### **Anxiolytics**

Current, aggressive therapies for cutaneous burn wounds, together with the persistent and repetitive qualities of background and procedural pain, make burn care an experience that is likely to cause anxiety in both adult and pediatric patients. It is also recognized that anxiety can worsen acute pain. This has led to the common practice in U.S. burn centers of using anxiolytic drugs in combination with opioid analgesics. Intuitively,

this practice is particularly useful in premedicating patients for wound care, due to the anticipatory anxiety experienced by these patients prior to and during debridement. Although previously shown that benzodiazepine therapy improves postoperative pain scores in non-burn settings, it has been recently reported that low dose benzodiazepine administration significantly reduces burn wound care pain reports. It appears that the patients most likely to benefit from this therapy are not those with high trait (premorbid) anxiety, but rather those with high state (at the time of the procedure) anxiety or those with high baseline pain scores.

## Anesthetics

Inhaled nitrous oxide is an analgesic agent safe for administration by non-anesthesia personnel. It provides safe and effective analgesia without loss of consciousness for moderately painful procedures in other healthcare settings, and is also a commonly used, although less well-studied agent for the treatment of burn pain. It is typically used as a 50% mixture in 50% oxygen, and is self-administered by an awake, cooperative, spontaneously breathing patient via a mouthpiece or mask. A secondary benefit of nitrous oxide use, like that of PCA opioid administration, is the element of control given to the patient for his/her care. Nitrous oxide is less useful with critically ill or uncooperative patients. It has also been implicated in a very small, but measurable incidence of toxicity issues (e.g., spontaneous abortion, bone marrow suppression) to patients or staff exposed for prolonged periods, although not in the setting of burn pain treatment. Some burn centers administer nitrous oxide only through a pain service, check B12 blood levels prior to use, and set limits to the duration and number of times used.

Although it is obvious that general anesthesia is required for the excision and grafting of deep burn wounds, there is a small population of patients who require specific wound care procedures on a scale well below that of surgical burn care, yet are difficult to perform on a conscious patient. These procedures include i) the removal of hundreds of skin staples from recently grafted wounds, ii) meticulous wound care of recently grafted, and often tenuous skin on the face or neck, and iii) wound care procedures in variably cooperative children (and adults). Historically, IV or intramuscular ketamine has been used for these procedures due to its potent analgesic and sedation properties, and more recently oral ketamine use is described for pediatric burn patients. However, ketamine use is limited by the potential risk of associated emergence delirium reactions (5-30% incidence), particularly in the elderly.

The extension of full anesthetic care capabilities outside of the operating room and into the burn unit has been implemented in some specialized burn centers with success. This has been facilitated by the recent introduction into clinical anesthetic practice of a variety of drugs with a rapid onset and short duration of action, a more rapid awakening/recovery, and fewer associated side effects -- ideal qualities for agents to be used for procedural burn wound care. These agents include IV propofol and remifentanyl, and inhaled sevoflurane. Propofol is particularly advantageous, and can be titrated to effect both in terms of level of consciousness and duration of action using continuous IV infusion techniques. The provision of brief, high potency analgesia/anesthesia in a comprehensively monitored setting by individuals specifically trained to provide the service appears safe and efficient, both in terms of allowing wound care to proceed rapidly under ideal conditions for patient and nursing staff, and in terms of cost-effective use of the operating room only for true surgical burn care procedures.

Local anesthetics are of obvious use in regional blockade for wound care procedures, but have also been used for burn pain analgesia as a topical gel or IV infusion. Topical local anesthetic use on the burn wound is controversial. Prilocaine-lidocaine cream (EMLA) has no effect on burn pain in volunteers; however, topical 5% lidocaine applied at 1 mg/cm<sup>2</sup> offers analgesic benefit without associated side effects. Topical lidocaine use is significantly tempered by reports of local anesthetic-induced seizures due to enhanced systemic absorption at the open wound site. The analgesic benefit of an IV lidocaine bolus (1 mg/kg) and 3-day continuous infusion (40 mg/kg/min) has also been reported acute burn injuries, although whether its mechanism is due to anti-inflammatory or analgesic actions is unclear. Administration of local anesthetics (and/or opioids) via epidural catheter would seem to be of benefit in patients with lower extremity burns, resulting in both analgesia (particularly during procedural burn care) and sympathectomy (of theoretical benefit to wound healing). However, such use has only been reported anecdotally. A major drawback of this technique is the use of an indwelling

catheter in patients densely colonized with infectious organisms at the wound site, thus increasing the risk for epidural abscess formation.

## **Background Pain Management**

Because background pain is relatively constant, it is best treated with mild-to-moderately potent analgesics administered so that plasma drug concentrations remain relatively constant throughout the day. Examples include the continuous IV infusion of fentanyl or morphine (+/- patient-controlled analgesia [PCA]), the oral administration of long-acting opioids with prolonged elimination (methadone) or prolonged enteral absorption (sustained-release morphine, sustained release oxycodone), or oral administration on a regular schedule of short-acting oral analgesics (oxycodone, hydromorphone, codeine, acetaminophen). Background pain decreases with time as the burn wound (and associated donor sites) heals, so that analgesics can be slowly tapered (in the absence of significant analgesic tolerance).

## **Procedural Pain Management**

In contrast to background pain, procedural pain is significantly more intense, but shorter in duration; therefore, analgesic regimens for procedural pain are best comprised of moderately-to-highly potent opioids that have a short duration of action. Intravenous access is helpful in this setting, with ketamine and short-acting opioids (fentanyl, alfentanil) offering a potential advantage over more longer-acting agents (morphine, hydromorphone). In the absence of IV access, orally administered opioids (morphine, hydromorphone, oxycodone, codeine) are commonly used, although their relatively long durations of action (2-6 hr) may potentially limit post procedure recovery for other rehabilitative or nutritional activities. Oral ketamine, oral transmucosal fentanyl, and nitrous oxide are agents of particular use when IV access is not present, due to their rapid onsets and short durations of action. Finally, when a particularly painful dressing change or one that requires extreme cooperation in a non-compliant patient (e.g., face debridement in a young child) is anticipated, the provision of brief general anesthesia in the burn unit setting has been shown to be safe and effective.

## **Postoperative Pain Management**

Postoperative pain deserves special mention because of the increased analgesic needs that should be anticipated following burn excision and grafting. This is particularly true when donor sites have been harvested, as these are often the principal source of increased postoperative pain complaints, rather than the grafted burn. Typically, this increased analgesic need is limited to 1-4 days following surgery before returning to preoperative levels.

## **Non-pharmacologic Approaches**

Perhaps the most powerful types of nonpharmacologic interventions are those that prevent or avoid unnecessary elements of care that may cause pain. For example, adequately soaking dressings can ease the pain of their removal. Providing calm care and offering patients some control during painful procedures can facilitate comfort during therapies and wound care.

Psychological techniques for acute pain control can include hypnosis, cognitive behavioral techniques, distraction and operant (learning) approaches. Hypnosis has been found to reduce burn pain in over a dozen studies. With this modality, a clinician typically works with patients before wound care or therapies and provides post-hypnotic suggestions for comfort. Cognitive-behavioral interventions work by restructuring patients' thoughts about pain. For example, patients may be taught that the sensations during therapy may hurt, but will not harm them. Distraction techniques may be as simple as movies, computer games or conversation during painful procedures or as elaborate as immersive virtual reality. A recent series of studies indicates that placing patients in a virtual world can dramatically reduce pain during wound care and therapies.

Behavioral (learning) techniques have a particularly important role in burn rehabilitation. Patients who are overwhelmed and resistant to therapies may show significant progress with the quota system.

The quota system rewards activity with rest after patients have reached predetermined markers of therapeutic activity (quotas) that are well within their capacity. In establishing quotas, therapists exercise patients for three sessions to the point of fatigue and then record the duration or number of repetitions. The average of these three sessions is calculated and then 80% of that average serves as a starting point. For example, a patient may walk 150, 50 and 100 feet over 3 sessions. The average (100 feet) is calculated and 80% of that (80 feet) serves as the starting point. The therapist then increases exercise by 5% each session. Importantly, even when the patient feels that s/he can keep exercising, increments are kept at 5%. This keeps exercise increments at steady rates and avoids overwhelming the patient.

Patients with chronic pain often respond well to techniques in which their pain behavior is ignored (their pain behavior, but not them) and they are distracted from pain. While acute pain necessitates immediate clinical attention, chronic pain often requires a reversal of strategies both in terms of medications and clinician response.

Pain complaints consistent with neuropathic pain can persist in burn patients despite complete closure and healing of both burned skin and donor sites; thus, centrally-acting non-opioid agents may have specific application in this fortunately uncommon setting. Antidepressants (e.g., amitriptyline), anticonvulsants (e.g., gabapentin) and clonidine have been proposed as potential analgesic agents for non-acute burn pain based on their known mechanisms of action in other chronic pain states (e.g., neuropathic pain). Although these agents have not been studied extensively in the setting of burns, various centers report anecdotal success with their use in these challenging patients. In contrast to opioids that produce analgesia by interacting with opiate receptors located primarily in the dorsal horns of the spinal cord and the periaqueductal gray region of the brainstem to modify nociceptive input, the mechanism of action of these other centrally acting agents is less well understood. It is presumed that their actions (e.g., gabapentin on central GABA receptors, clonidine on central alpha-2 receptors) inhibit ectopic neuronal activity in damaged primary neurons unrelated to nociception that can be perceived by neuropathic patients as pain.

## References

Loeser, J. (Ed.). (2001). *Bonica's Management of Pain* (3rd ed.). Philadelphia, PA: Lippincott, Williams & Wilkins.

## Legends

Figure 1: Harborview Medical Center/University of Washington Burn Center burn analgesic guidelines for adults. Analgesic and anxiolytic choices are simplified to a minimum number of agents to encourage staff familiarity, and are targeted to specific pain and anxiety needs. Therapy can be individualized to include agents not in this guideline when clinically indicated. This chart is laminated and prominently displayed in all patient care areas. (MS = morphine sulfate; IV = intravenous; NSAIDS = non-steroidal anti-inflammatories; Nitrox = 50% nitrous oxide/ 50% oxygen inhaled)