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PAIN MANAGEMENT IN TRAUMA (MR HOFFMAN, SECTION EDITOR)

# Acute Pain in the Trauma Patient

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## Abstract

**Purpose of Review** This review will discuss the unique challenges associated with pain control in the trauma patient. Trauma is accompanied by painful conditions such as fractures, surgery, and nerve injury, but the trauma population also provides additional challenges compared to the general hospitalized population with respect to pain control because of the acute stress reaction and other psychological responses to trauma, often underlying chronic pain, and the increased risk of opiate use at baseline in this population.

**Recent Findings** The importance of recognizing uncontrolled pain early is essential to prevent adverse acute and chronic outcomes including post-traumatic stress disorder, transition to chronic pain, delirium, and respiratory failure.

**Summary** A true multimodal approach to pain control in trauma patients includes early evaluation and consideration of techniques such as epidural anesthesia as well as nerve and fascial blocks, the use of non-opiate medications in addition to opiate medication, and early evaluation for uncontrolled stress, anxiety, and risk factors for post-traumatic stress disorder.

**Keywords** Acute pain · Trauma · Multimodal therapy · Post-traumatic stress disorder · Opioid use disorder

## Introduction

The trauma patient provides a unique challenge in managing acute pain. Pain in trauma stems from the chemical propagation of pain from injury, as well as the acute stress reaction from the traumatic event or injury that can create emotional distress that contributes to pain. In addition, because substances such as opiates increase the risk of traumatic injury, a higher percentage of the trauma population has narcotic tolerance or takes opiate pain medication at baseline than the general population. Traumatic injury is also an independent risk factor in developing persistent opiate use, which can transition to illicit use in up to 5% of chronic opiate users [1, 2••].

In spite of these challenges, managing acute pain effectively in the trauma patient is crucial. In these patients, background pain can be easier to treat than evoked pain; however, pain control of both is necessary. Poor control of acute pain is linked to a higher risk of developing chronic pain, longer and more delayed recovery, and worse quality of life [3•]. Inadequate pain control can lead to an altered release of hormones including insulin and catecholamines, metabolic disturbances, water retention, increased myocardial oxygen demand, agitation, delirium, delayed wound healing, hypoxia/atelectasis, and neuropsychiatric complications such as isolation, anxiety, and PTSD, which can lead to chronic pain [2••].Of note, patient-reported satisfaction does not correlate with absolute pain scores, but rather with a reduction in pain scores. Thus, a pain reduction from an 8 to a 6 may provide the same satisfaction in care as a reduction from a 4 to a 2 [4].

This chapter will review medications for pharmacologic pain emphasizing opioid-sparing analgesia, regional anesthesia techniques and their potential in the trauma population as well as nonpharmacologic methods.

## Pharmacologic Pain Control

### NSAIDs and Acetaminophen

Over the counter pain relief medications such as nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen have a key role in a multimodal pain regimen. NSAIDs reduce pain

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through the anti-inflammatory effects of cyclo-oxygenase 1 and 2 (COX 1 and 2) receptors. Other effects include antiplatelet properties and antipyretic effects. Antiplatelet effects are tied to the COX 1 receptor, so some NSAIDs such as celecoxib are COX 2 specific to decrease bleeding risk [1]. Well-known adverse effects include gastrointestinal symptoms such as bleeding and gastritis, renal failure, increased risk of MI and stroke, and impaired bone healing [3•].

Of significance in the trauma population is the effect of NSAIDs on bone healing. A retrospective study of all femur, tibia, and humerus fractures at a level 1 trauma center by Jeffcoach et al. found that patients with long bone fractures who received NSAIDs were twice as likely to have bone healing complications such as nonunion or infection. For reference, smokers were three times likely to have bone healing complications [5]. Nonunion and bone fracture healing appear to have a dose-dependent relationship. However, this relationship between nonunion and NSAIDs has not been confirmed in prospective studies for short courses of anti-inflammatory medication (< 6 weeks) [1]. Given this, the risk of impaired fracture healing associated with NSAID use should be considered in patients with multiple fractures especially in cases where nonunion would have serious clinical relevance, for example in C-spine fractures; however, NSAIDs are a viable option for pain control in many trauma patients.

NSAIDs also carry a black box warning describing an increased risk of heart attack or stroke after a few weeks of starting NSAID therapy. This risk appears to be minimal in shorter courses. As NSAIDs reduce kidney blood flow, they are contraindicated in patients with acute kidney injury or with significant pre-existing renal insufficiency. Although some selective COX-2 inhibitors have been withdrawn off the market previously due to increased cardiovascular risk, a large prospective trial of celecoxib revealed equivalent safety to ibuprofen or naproxen [1]. GI bleeding and gastritis are other notable adverse effects of NSAID therapy.

Acetaminophen is another over-the-counter analgesic that works through the COX3 receptor to ameliorate pain [2••]. Acetaminophen is often given with narcotics as it can decrease opiate requirements by up to 20% thus decreasing opiate induced side effects such as nausea and oversedation [6]. Notably, although it significantly decreases opiate use, it is not found to decrease pain scores [1]. Tylenol is available in IV, oral, and rectal forms, with limited advantage of the more expensive IV formulation beyond faster onset of action and ability to give this formulation in patients unable to take in PO [3•]. Due to risk of hepatotoxicity, acetaminophen dose should be limited to 4 g daily in healthy, average-sized adults and limited to 2 g daily in patients with hepatic dysfunction such as cirrhosis.

The importance of the commonly taken over medicines such as acetaminophen and NSAIDs in a multimodal pain regimen cannot be undersold. Randomized control trials of emergency department patients given either 400 mg of ibuprofen and 1000 mg of tylenol, 5 mg oxycodone and 325 of acetaminophen, 5 mg of hydrocodone and 300 mg of acetaminophen, or 30 mg of codeine and 300 mg of acetaminophen showed no statistically or clinically significant differences in pain score reductions after 2 h between tylenol/ibuprofen and any opiate pain medication [7]. We feel strongly that any multimodal pain regimen should include NSAIDs and acetaminophen in appropriate candidates.

### Gabapentin

Gabapentin has been well studied as a medication that can decrease opiate consumption and decreases the chance of progression from acute pain to chronic pain. Initially released as an anti-seizure medication in 1993, gabapentin works through inhibiting the alpha-2-delta subunit of voltage-gated calcium channels, causing decreased influx of calcium, and decreased release of glutamate and substance P [3•]. The use of gabapentin has tripled in the past 15 years, especially in attempting to decrease narcotic use in patient's prescribed opiates for chronic pain [8].

A randomized controlled study of 120 trauma patients with peripheral nerve injury showed that although there was no significant difference in pain score between the gabapentin and placebo group, there were statistically significant amounts of patients with at least a 30% reduction in pain and improved pain relief in the group receiving gabapentin [9]. There has been an interest in the literature in using gabapentin and pregabalin to decrease perioperative opiate requirements in the surgical population. A 2018 randomized control trial by Hah et al. of gabapentin 1200 mg preoperatively and 600 mg TID postoperatively versus lorazepam and placebo showed that gabapentin does not affect time to pain resolution (a pain score of 0/10). However, it does increase the rate of opioid cessation by 24% with no significant differences in adverse effects, indicating utility in decreasing opiate requirements [10].

Single-dose perioperative pregabalin has been shown to decrease postoperative opiate requirements, although there is a question in the literature about the optimal timing and duration of dosage [3•]. One meta-analysis of pregabalin use in patients undergoing laparoscopic cholecystectomy found that usage of pregabalin in the perioperative period helped reduce postoperative pain, morphine consumption, and opioid-related complications [11]. Some studies have shown evidence that a short course of gabapentinoid increases the rate of stopping opioid consumption after surgery [1].

However, a recent randomized controlled trial of 40 patients with rib fractures receiving gabapentin vs placebo for 1 month yielded no differences in pain control or quality of life at 1 month out from injury [12], indicating that more research is needed for indications for gabapentin for the treatment of acute pain versus using gabapentin for prevention of

the transition from acute to chronic pain and to encourage cessation of opiate usage.

Adverse effects of gabapentin and pregabalin include somnolence, visual disturbance, and dizziness. Limitations to gabapentin use include the lack of IV form and gabapentin's selective duodenal absorption, giving it less utility in the critically ill patient population [2••]. In the setting of the opiate epidemic, there has also been increasing evidence of gabapentinoid misuse, ranging around a 1% for population prevalence and even higher in patients suffering from opioid misuse. Law enforcement reports have also reported increased street demand for gabapentinoids [8].

### Muscle Relaxants and Benzodiazepines

Muscle relaxants such as cyclobenzaprine, carisoprodol, tizanidine, baclofen, and orphenadrine have limited data in the trauma population. There have been reports of improvement of spasticity with baclofen and tizanidine for spinal cord injuries [3•]. Muscle relaxants have limited data in the postoperative care literature, one randomized control trial after inguinal hernia repair reported tizanidine helped decrease postoperative pain scores significantly and was associated with earlier return to normal activity [13].

These medications should be used with caution in the elderly as they can be sedating and there is abuse potential with these medications. Orphenadrine is a skeletal muscle relaxant with less sedating effects than others, but is less commercially used and therefore has very limited data around its use.

Like muscle relaxants, benzodiazepines have been shown to decrease spasticity, which can especially benefit spinal cord patients. In addition to this, benzodiazepines help to decrease the fear of future pain such as prior to a procedure [3•]. However, much like opiates, dependence to benzodiazepines forms quickly, they increase the risk of delirium, and there is a high risk of oversedation and drowsiness with their use [13].

### Alpha 2 Agonists

These medications may have benefit in acute pain as a way to decrease opiate requirements [3•]. Alpha 2 agonists such as clonidine and dexmedetomidine are thought to have pain control properties through activation of postsynaptic alpha 2 adrenoceptors of the noradrenergic pathways [2••]. Clonidine has the advantage of more antianxiolytic properties as well as a longer-acting medication [2••, 3•]. Clonidine is used as an analgesic in some European countries such as Germany. Dexmedetomidine also has been studied to have decreased opiate use, as well as a decreased risk of delirium and shorted ICU stay [3•]. Significant side effects include hypotension and bradycardia.

### IV Lidocaine

Although widely used topically, there is increasing data for the use of lidocaine as systemic anesthesia, through infusions or bolus dosing. Lidocaine is in the amide subcategory of local anesthetics and has a half-life of approximately 60–120 min. It is thought to contribute to pain control through reversible sodium channel blockade that decreases nerve propagation. Meta-analysis of 536 patients treated with IV lidocaine in the emergency department showed noninferiority in two out of six RCTs and superiority to morphine in two trials [14]. One small randomized control trial of 40 emergency department patients revealed IV lidocaine given at 2 mg/kg was found to have more significant pain reduction to IV morphine at 15 and 30 min post-infusion in cases of critical limb ischemia [15].

This same analysis yielded 20 adverse effects out of the 225 patients included in randomized controlled trials, including one serious complication of a seizure leading to bradycardia and cardiac arrest [14]. IV lidocaine has been dosed as 1–2 mg/kg bolus, a fixed bolus of 50–100 mg, or a 1 mg/kg per hour infusion [16]. Notably, more trials, specifically randomized controlled trials, are needed for effective recommendations for IV lidocaine, specifically dosage and recommendations in patients with preexisting heart disease, given the antiarrhythmic properties of IV lidocaine and the potential for cardiac symptoms to be the first sign of toxicity when lidocaine is given as a bolus [14].

### Ketamine

Ketamine is a phencyclidine analog and dissociative anesthetic agent that has gained recent popularity for the treatment of acute pain in addition to its anesthetic properties. Analgesia properties of ketamine stem from reversible antagonism of N-methyl-D-aspartate receptor. Although used in the treatment of chronic pain through reversing central sensitization, recent research has shown effectiveness in treating acute pain in conditions as diverse as sickle cell crises, renal colic, and trauma [17•].

When using ketamine for acute pain, it is important to distinguish that this is done at subanesthetic doses. In anesthetic doses as defined by the FDA as 1 to 4.5 mg/kg, the guidelines recommend subanesthetic dosing at a maximum of 0.3 mg/kg bolus, possibly with a concomitant infusion at a maximum of 1 mg/kg/h outside of situations with intensive monitoring.

Recent consensus guidelines from the American Society of Anesthesiologists recommend considering patients for subanesthetic ketamine treatment who are undergoing surgery with severe pain, opioid-tolerant patients with exacerbations of pain or needing surgery or other painful procedure, and in patients at risk for opiate-induced respiratory depression, such as patients with obstructive sleep apnea.

In the opioid-tolerant population, studies have shown benefits such as better pain control and possibly decreased opiate use as far out as 6 weeks out from surgery [18]. Infusions of subanesthetic dose ketamine (0.06–0.3 mg/kg/h) has been shown to decrease opiate requirements in surgical intensive care unit patients. A recent meta-analysis of randomized control trials using ketamine in spine surgery by Pendi et al. found that ketamine decreased postoperative opiate requirements in the first 24 h and resulted in improved pain control, with no statistically significant adverse effects [19].

It is important to note that more research is needed on the effects of ketamine in the pediatric population, as some studies have shown no decrease in opioid requirements when subanesthetic ketamine is used as a part of the anesthetic regimen [17•]. The consensus guidelines also advised that poorly controlled cardiovascular disease, pregnancy, severe hepatic dysfunction, and active psychosis are contraindications to ketamine use for pain control. Elevated intracranial pressures and elevated intraocular pressures were also listed as contraindications, although the assertions that ketamine increases these pressures have been called into question [2••].

Adverse effects of ketamine are most commonly nausea, vomiting, vivid dreams or hallucinations, and much more rarely dissociative symptoms. There is very limited data to support oral or intranasal ketamine in the setting of acute pain, but it can be tried for patients with difficult IV access or children. There were no recommendations for a pure ketamine PCA, although ketamine combined with an opiate PCA can help decrease opiate requirements [17•].

### Opioids and the Opioid-Tolerant Patient

The FDA defines opioid-tolerant as a patient that for at least 1 week has been ingesting greater than or equal to oral morphine at 60 mg per day, transdermal fentanyl at 25 mcg per hour, oral oxymorphone at 25 mg per day, oral hydromorphone at 8 mg per day, or any equivalent dose.

Studies have shown that one-third of patients prescribed opioids for chronic pain misuse their medication and around 5% of these patients eventually transition to heroin use. As mentioned earlier, the trauma patient population is unique in that opiate use (and misuse) predisposes to injury and trauma, so a higher percentage of the trauma patient population have had exposure to opiates at baseline or can be classified as opiate tolerant prior to injury. Approximately 16–20% of trauma patients take opiate medication prior to injury [2••].

Despite these risks and pre-exposure, opioids still have a role as a part of a multimodal pain approach in the trauma population. Specific opiates' role in the pain control plan depends on the patient's previous exposure to opiates, level of pain, and hemodynamics. Fentanyl is particularly useful in the acutely ill due to its potency, 1–2 min time to onset of action, and short half-life of less than 60 min. Fentanyl also differs from other opiates in that it has minimal vasodilatory effects and therefore is the first line for pain relief in hemodynamically unstable trauma patients [2••]. Other options include morphine and hydromorphone with both oral and IV formulations, and oxycodone, hydrocodone, and tramadol for oral options.

The adverse effects of opiates are serious, meaning analgesia plans in the trauma patient should be continually evaluating for ways to mitigate pain to decrease opiate use. Adverse effects of opioids include nausea, respiratory depression, urinary retention, ileus, increases in intensive care unit (ICU) delirium, and potentially osteoporosis [2••, 3•]. Opioid-induced hyperalgesia is thought to be due to alterations in the processing of pain signals caused by the medication, leading to opiate use, especially prolonged use, causing increased sensitivity to pain and even misinterpretation of nonpainful stimuli as painful. Addiction and dependence are also significant risks of opioid use, especially given the evolving opioid crisis.

With all medications, it is important to note altered drug effects in critically ill patients due to physiology of critical illness, such as ileus, acid-base derangements, altered splanchnic blood flow, and drug-induced worsening of organ dysfunction [2••].

## Interventional and Procedural Analgesia Techniques

Procedure-based anesthesia techniques have gained popularity in the trauma patient population in recent years, both for associations with better outcomes and with helping reduce opioid use. These regional anesthesia techniques can be divided into neuraxial blocks such as subarachnoid and epidural anesthesia, peripheral nerve blocks to target a specific nerve, or fascial plane blocks like transversus abdominis plane (TAP) blocks providing pain relief to a specific dermatome. Table 1 provides a complete list of examples of these.

Epidural anesthesia and erector spinae blocks have gained increased popularity in cases of traumatic rib fractures. Aggressive use of these methods as a way to reduce opioid use has been found to decrease PTSD occurrence can have fewer opioid-induced complications such as nausea or respiratory depression, and fewer days in the ICU [2••].

In one larger retrospective cohort study of blunt thoracic trauma patients between ages 18 and 84 by Gage et al., epidural catheter placement was associated with decreased risk of dying in patients with blunt thoracic trauma of 3+ rib fractures without increased risk thrombotic complications such as DVT or PE. Although epidural anesthesia was initially hypothesized to decrease mortality through decreasing pulmonary complications such as pneumonia and empyema, this study found that there was actually no significant difference in pulmonary complications in patients receiving epidural anesthesia and those not. After review of the data, it is theorized that

**Table 1** Summary of interventional anesthesia techniques

| Block type | Mechanism | Examples | Contraindications |
|---|---|---|---|
| Neuraxial anesthesia | Medication in epidural or subarachnoid space in order to provide analgesia to a specific spinal level | -Epidural anesthesia<br>-Spinal anesthesia | -Coagulopathy<br>-Inability to position to place |
| Fascial block | Block area of fascia to provide pain relief to a dermatome | -Erector spinae block<br>-Transversus abdominus block<br>-Serratus anterior plane block | -Theoretical potential to mask severe increases in pain that accompany serious complications such as compartment syndrome |
| Peripheral nerve block | Aims to block a specific nerve | -Axillary block<br>-Digital nerve block<br>-Lumbar plexus block<br>-Femoral nerve block<br>-Intercostal nerve block | Few absolute indications, some relative include active infection at the site of block, preexisting neural deficits at the site of the block. |

epidural catheters decrease opioid use, decrease delirium, and cause a reduction in sympathetic hyperactivity that results in decreased mortality. An important potential confounder of this study is that most epidural catheters were administered at level 1 trauma centers, which is already associated with improved outcomes [20].

The use of epidural anesthesia in rib fractures in the elderly has been associated with reduced rates of delirium [2••]. Other meta-analyses have not found significant evidence for the use of epidural anesthesia in the blunt thoracic trauma population [21, 22], underscoring the need for more investigation with larger studies and more randomized controlled trials to explore the potential benefit of epidural anesthesia in the blunt thoracic trauma population.

Contraindications to epidural anesthesia include coagulopathy, inability to position for placement, need for aggressive VTE prophylaxis, altered mental status, and risk of hemodynamic instability associated with the sympathetic blockade [2••]. Fascial plane blocks such as the TAP block or erector spinae plane blocks present an option for similar anesthesia techniques with a better side effect profile that can be performed in more coagulopathic patients than epidural anesthesia.

Fascial plane blocks use infusions of local anesthetics or other medications to provide pain relief for specific dermatomes. These are not associated with the risks of hypotension as neuraxial anesthesia and can be done in more coagulopathic patients. The erector spinae block emerged in 2016 as a regional block for thoracic nerve pain as an alternative to epidural anesthesia that shows promise in the thoracic trauma population. Although there are still modifications being made to this new technique, a review of 242 cases found that the typical technique included an initial dose with repeat boluses later. This found that this technique, when used with multimodal anesthesia, provided a promising option for rib fracture pain relief, with 34.7% of cases having a reduction in opioid use, and only one adverse event (pneumothorax) [23].

Several new products such as the On-Q pain relief system and Ambu action fuser have used the concept of regional blocks such as the ESP and TAP blocks to formulate pain relief systems that attempt to provide more long-lasting pain relief of a dermatome. These systems typically involve the implantation of a catheter near the fascia connected to a patient-controlled button that dispenses a local anesthetic infusion to this region. This can provide several days of the effects of a plane block and provide a promising route to help reduce opioid requirements. Patients can also be instructed on how to remove the catheter, and can therefore be sent home with these products to help reduce the amount of opioid prescribed at discharge. In addition to the contraindications of regional blocks and risk of infection with any implant, there have been studies linking these systems to longer hospital stay after knee arthroplasty [24]. There is also an increased risk of infection, given this is an implantable device, and some studies have found that their improvements in pain score are not significant past postoperative day 1 [25].

Peripheral nerve blocks that target a specific nerve have gained popularity as well. These are especially useful in isolated orthopedic injuries and can sometimes be used to avoid general anesthesia in patients at high risk for complications from general anesthesia. The main complication of these blocks is the theoretical risk that it may mask serious complications such as compartment syndrome; however, prospective studies have not shown this. However, case reports of compartment syndrome in patients with nerve blocks have shown that these patients present with breakthrough pain that is significant even with the block present. Anticoagulation is a relative contraindication, especially in attempts to block deep nerves in uncompressible locations [1].

Although there is more research needed to explore the risk vs benefit profile in regional anesthesia techniques in some patient populations, the potential to decrease opiate use and the serious complications of opioid-induced respiratory depression and opioid tolerance and dependence make these regional anesthesia techniques a valuable tool in the

traumatologist's arsenal, especially in the already opioid-tolerant patient.

Traumatic wounds of many kinds can cause significant evoked pain both during movement and medical procedures, as well as background pain that persists around the clock. Dressing changes can be extremely painful. The most basic approach to minimizing wound pain is the use of appropriate dressings that are minimally painful in application and removal, such as non-adherent dressings. Lidocaine and lidocaine hydrochloride are used as topical analgesics both on intact skin, mucous membranes, and wounds, especially for pain relief during medical procedures. Intra-wound application of lidocaine has also been studied in its ability to decrease pain of vacuum-assisted closure (VAC) dressing removal. In this study, patients who had their VAC sponge injected with 1% lidocaine solution reported less pain and used less narcotics than when a saline placebo was used. [26] Lidocaine has been shown to be able to provide meaningful pain relief when applied to an open wound.

### Nonpharmacologic Methods

Although much of the research on pain in the trauma patient focuses on pharmacologic intervention, pain is a subjective experience inextricably linked to emotions such as anxiety and fear that stem from trauma and the unfamiliar landscape of the inpatient hospital that each patient experiences. Trauma is naturally associated with an acute stress reaction depending on the specific event that led to injury and the patient's existing coping skills for dealing with these events. For example, literature search reveals that nearly 16% of victims of road accidents suffer from acute stress disorder, which is a predictor of continued mental health problems in the future, most commonly post-traumatic stress disorder [27, 28].

Techniques such as distraction while performing painful medical procedures, presence of family and friends for emotional support, and potentially cognitive behavioral therapy in patients who are at high risk for PTSD [27] cannot be underscored as methods to decrease emotional distress and therefore decrease the perception of pain. A meta-analysis of 45 observational and 21 interventional studies found that patients with complex social problems such as low social support, financial problems, low income, and lower cognitive functioning patients, those with psychological disorders at baseline, and younger, female patients were most likely to have acute stress disorder or PTSD symptoms. [28] In patients with risk factors such as these as well as symptoms, cognitive behavioral therapy (CBT) has been shown as the most effective method to prevent PTSD [28].

## Conclusion

Trauma is accompanied by painful conditions such as fractures, surgery, and nerve injury, and the trauma population provides additional challenges compared to the general hospitalized population with respect to pain control because of the acute stress reaction and other psychological responses to trauma, often underlying chronic pain, and the increased risk of opiate use at baseline in this population. The importance of systems and nursing protocols to frequently assess pain and recognize uncontrolled pain early is important to prevent adverse acute and chronic outcomes of uncontrolled pain including PTSD, transition to chronic pain, worse quality of life, delirium, and respiratory failure. A true multimodal approach to pain control in these patients includes early evaluation and consideration of techniques such as epidural anesthesia as well as nerve and fascial blocks, the use of non-opiate medications in addition to opiate medication, and early evaluation for uncontrolled stress, anxiety, and risk factors for PTSD with interventions such as CBT.

### Compliance with Ethical Standards

**Conflict of Interest** Dr. Reed and Dr. Schurr have no conflicts of interest or disclosures to report with respect to the facts presented in this article.

**Human and Animal Rights and Informed Consent** All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards.

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