Pain management in neurocritical care; an update

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\textbf{Purpose of review}  
Pain management in neurocritical care is a subject often avoided because of concerns over the side-effects of analgesics and the potential to cause additional neurological injury with treatment. The sedation and hypercapnia caused by opioids have been feared to mask the neurological examination and contribute to elevations in intracranial pressure. Nevertheless, increasing attention to patient satisfaction has sparked a resurgence in pain management. As opioids have remained at the core of analgesic therapy, the increasing attention to pain has contributed to a growing epidemic of opioid dependence. In this review, we summarize the most recent literature regarding opioids and their alternatives in the treatment of acute pain in patients receiving neurocritical care.

\textbf{Recent findings}  
Studies on pain management in neurocritical care continue to explore nonopioid analgesics as part of a multimodal strategy aimed at decreasing overall opioid consumption. Agents including local anesthetics, acetaminophen, ketamine, gabapentinoids, and dexmedetomidine continue to demonstrate efficacy. In addition, the prolonged longitudinal course of many recent trials has also revealed more about the transition from acute to chronic pain following hospitalization.

\textbf{Summary}  
In an era of increasing attention to patient satisfaction mitigated by growing concerns over the harms imposed by opioids, alternative analgesic therapies are being investigated with promising results.

\textbf{Keywords}  
acute pain, craniotomy, neurocritical care, opioid safety, spine surgery, subarachnoid hemorrhage

\textbf{INTRODUCTION}  
The neurological examination provides a window into the vitality of the central nervous system. In order for clinicians to optimize the treatment of acute neurological disease, great effort is made to avoid all interventions which can blunt the neurological examination and thereby undermine the detection of responses to medical therapy. As acute pain can be symptomatic of neurological deterioration, analgesic therapies have historically been withheld from patients with acute neurological disease. Furthermore, after the discovery of the endogenous opioid receptor and its antagonist, naloxone, researchers endeavored to improve the neurological examination by administering naloxone to patients with acute spinal injuries and subarachnoid hemorrhage [1,2]. Although such efforts ultimately failed to improve the treatment of acute neurological disease, they highlight the historical ambivalence held toward analgesics, specifically opioids, by the neurocritical care community.

Opioids, which are the mainstay of acute pain management pose several risks to patients, particularly those with neurological disease. In addition to blunting the detection of pain as a symptom, opioids also cause miosis and sedation which may confound the ability to determine whether a clinical change is because of the medication or the patient’s neurological status [3]. The sedative effects of opioids are more pronounced in elderly patients and can be prolonged in those with coexisting renal or hepatic impairment [4]. The induction of sedation by opioids has been attributed to an anticholinergic effect in an experimental animal model, and is not likely to represent the effect of analgesia alone [5]. In addition to masking the neurological examination, opioids can cause respiratory depression. The hypoxia caused by
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KEY POINTS

- Opioids pose significant short-term and long-term risks to patients recovering from acute neurological conditions.
- Research into the efficacy of opioid-sparing analgesics has provided some promising results, especially in the context of multimodal analgesia.
- Longitudinal pain studies continue to demonstrate the lasting effects of pain following hospitalization in neurocritical care.

Opioids pose significant short-term and long-term risks to patients recovering from acute neurological conditions. Longitudinal pain studies continue to demonstrate the existence of moderate to severe pain even after craniotomy that is typically more intense even after craniotomy that is typically more intense. Whether the treatment of postoperative pain is managed by the regulated dosing of opioids with patient-controlled analgesia (PCA) or by scalp nerve blockade, the number of other analgesics remains limited [9–11]. NSAIDs offer proven efficacy, yet platelet inhibition renders their use prohibitive in neurosurgical patients and patients with neurovascular disease. Although acetaminophen is an important adjunct in pain management, its cumulative dosing is limited because of the risk of liver toxicity. The evidence for opioids and their alternatives in the management of headache in neurocritical care will be described further in the following sections.

As the management of headache and pain overall remain a topic of growing interest and debate within the neurocritical care community, the subject of opioid dependence that more commonly afflicts patients recovering from spine surgery has been declared a national epidemic within the United States. The concept of ‘failed back syndrome’ has even been devised to describe patients that undergo technically faultless spine surgery, yet develop chronic pain that is not improved with subsequent revision surgery. The transition from acute to chronic pain may therefore not be caused by surgery alone, but by medical management, heavily based on opioid therapy, that often begins in neurocritical care. Accordingly, a growing call to manage postsurgical pain with alternatives to opioids is being made in an effort to reduce the risk of opioid-dependent pain [12]. The advent of multimodal analgesic strategies such as the enhanced recovery after surgery protocols, intended to minimize the overall opioid burden by combining different classifications of analgesics may also prove useful in addressing the opioid epidemic. The studies evaluating opioids and their alternatives following spine surgery will be discussed further in the subsequent sections.

HEADACHE

The causes for postcraniotomy headache have been attributed to the dissection of muscle, generation of inflammatory bone dust, dural traction, cerebrospinal fluid loss, and even direct injury to scalp nerves [13]. Many studies have suggested the incidence of moderate to severe pain to be in the range of 50–80% for the first 24–48 h postcraniotomy, underscoring the need to improve management [8,14,15]. In addition, the incidence of chronic incisional pain has been shown to be surprisingly high: 33–44% for acoustic neuromas and 17.5–29.3% for supratentorial craniotomies across multiple studies [15]. According to another estimate, 56% of patients experience chronic headache and 25% neuropathic pain 2 months after craniotomy [16].

Studies in the last decade have concentrated on several modalities, including acetaminophen, NSAIDs, cyclooxygenase-2 inhibitors, tramadol, dexmedetomidine, lidocaine infusion, gabapentinoids, scalp infiltration, scalp blockade, and transcutaneous electric acupuncture stimulation. These studies have been well described by multiple reviews and meta-analyses [12,17,18]. A review of the literature for the past 18 months divulged only a modest expansion in the existing knowledge base on the order of seven studies (Table 1).

Local anesthetics

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Table 1. Summary of analgesic trials on headache in neurocritical care

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population (N)</th>
<th>Intervention</th>
<th>Findings</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Can et al.</td>
<td>Craniotomy (90)</td>
<td>0.5% bupivacaine (B), 0.5% levobupivicaine (L), control (C) for scalp blockade</td>
<td>Decreased VAS in B and L at 2 h. No difference at other time points or in numbers of patients requiring additional analgesics postoperatively</td>
<td>No detail of numbers of supratentorial vs. infratentorial procedures. No mention of cumulative breakthrough analgesic doses (only number of patients needing treatment at predefined time points)</td>
</tr>
<tr>
<td>Jose et al.</td>
<td>Supratentorial craniotomy (90)</td>
<td>Dexamethasone 8 mg (2 ml) or saline added to 10 ml 2% lignocaine/30 ml 0.2% ropivacaine and epinephrine for scalp blockade</td>
<td>Dexamethasone provided no benefit to time to first rescue analgesic</td>
<td>Only noted time to first rescue analgesic. No VAS scores or cumulative analgesic doses. Stopped for futility</td>
</tr>
<tr>
<td>Akcil et al.</td>
<td>Infratentorial craniotomy (47)</td>
<td>0.5% bupivacaine scalp block (S) vs. pin sites/incisional infiltration (I) prior to frame placement vs. control. Only remifentanil given as intraoperative opioid in all groups</td>
<td>VAS score at 2 h lower in S group. Total morphine consumption at 24 h lower in I and S compared with control</td>
<td></td>
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<tr>
<td>Peng et al.</td>
<td>Supratentorial craniotomy (94)</td>
<td>Lidocaine 1.5 mg/kg bolus and 2 mg/kg/h vs. control</td>
<td>At the time of PACU discharge, lidocaine group had significantly more patients reporting no pain (NRS 0).</td>
<td>Patient transported to PACU with sufentanil PCA (2 mcg/h; 0.5 mcg, 15-min lockout). Tramadol given for breakthrough pain in PACU. 14 patients did not complete study. 80 study participants were analyzed</td>
</tr>
<tr>
<td>Dilmen et al.</td>
<td>Supratentorial craniotomy (83)</td>
<td>i.v. dexketoprofen, paracetamol, metamizol, or control administered at skin closure and at set intervals for first 24 h</td>
<td>No differences in 24 h morphine usage administered via PCA. No differences in VAS at predefined time points for 24 h</td>
<td>No safety concerns documented</td>
</tr>
<tr>
<td>Rajan et al.</td>
<td>Craniotomy (142), 58% supratentorial, 42% infratentorial</td>
<td>Intraoperative dexmedetomidine (D) 0.5–1 mcg/kg IBW load over 15 min and 0.2–0.7 mcg/kg/h vs. remifentanil (R) 0.08–0.15 mcg/kg/min</td>
<td>VAS pain score and total morphine equivalents administered significantly favored D for the initial 90-min postoperative period</td>
<td>D discontinued after patient’s head removed from pins. D discontinued at bone closure (about 30 min before surgery end time). Fentanyl 1–3 mcg/kg given on induction and 50 mcg during bone flap closure</td>
</tr>
<tr>
<td>Zhao et al.</td>
<td>Craniotomy (150), 87% infratentorial, 13% supratentorial</td>
<td>Dexmedetomidine [D] 0.6 mcg/kg vs. normal saline control (C). Propofol bolus 0.5 mg/kg ± infusion as needed for SAS 3–4 target. Fentanyl 50 mcg boluses as needed for pain</td>
<td>Time at target sedation, number of patients requiring rescue propofol and fentanyl, and total dose of fentanyl all significantly favored D. VAS immediately before extubation (median value 1 vs. 4, D vs. C) and 30 min after (median value 1 vs. 3, D vs. C) favored D</td>
<td>Study drug infusion initiated 2 h after end of surgery in the ICU. Nine patients in the D group required urgent discontinuation of the study drug because of SAS ≤ 2. No discussion on what triggered fentanyl administration. VAS only reported up to 30-min postextubation</td>
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IBW, ideal body weight; PACU, post-anesthesia care unit; PCA, patient-controlled analgesia; SAS, sedation agitation scale; VAS, visual analog scale.
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blockade being performed preoperatively (three studies) or after wound closure (four studies) revealed a reduction in postoperative pain scores up to 8 and 12 h, respectively. Pooled data demonstrated a reduction in morphine consumption for the first 24 h [26].

Three studies on scalp infiltration and scalp blockade were located over the period of interest. In the first study, bilateral scalp blocks were performed with 0.5% bupivacaine, 0.5% levobupivacaine, or controls (n = 30 in each group) prior to pinning. VAS was significantly better in the local anesthetic groups only at 2-h postoperative (Table 1) [19]. A second study assessed the utility of the addition of dexamethasone to the scalp blockade injectate. There was no benefit in any endpoint, including intraoperative opioid consumption or time to first analgesic request postoperative (Table 1) [20]. In the third study, 0.5% bupivacaine at pin sites/incisional infiltration were compared to scalp blockade (all procedures performed prior to pinning) and control in infratentorial craniotomy patients, with all groups receiving remifentanil as their only intraoperative analgesic. VAS scores were lower for up to 2 h in the scalp block group compared with control. Twenty-four-hour morphine consumption via PCA was significantly lower in both experimental groups (Table 1) [21]. In another study assessing the effects of intraoperative lidocaine infusion, patients in the lidocaine group had less pain at the time of postanesthesia care unit (PACU) discharge (Table 1) [22].

NSAIDS

In supratentorial craniotomy patients, administration of intravenous (i.v.) dexketoprofen 50 mg, acetaminophen 1 gm, or metamizole 1 gm at the time of wound closure and at appropriate dosing intervals for the first 24 h, did not impact cumulative 24-h morphine dosage compared with controls (Table 1) [23].

Dexmedetomidine

Two studies evaluated the use of dexmedetomidine on postcraniotomy pain. In the first study, intraoperative infusion of dexmedetomidine was compared with remifentanil. All endpoints significantly favored dexmedetomidine (Table 1) [24]. In the second study, dexmedetomidine was compared with saline controls in patients who required postoperative mechanical ventilation. Propofol and fentanyl were utilized as rescue agents for agitation and pain respectively (targeting a sedation agitation scale score of 3–4). Once again, most endpoints, including postextubation VAS, favored dexmedetomidine (Table 1) [25]. These studies were published shortly after novel data on dexmedetomidine which laid the foundation for exploring the utility of this agent for postcraniotomy pain. The former studies were impressive, revealing improved pain scores in the PACU and up to 12 h on the ward, as well as reduced opioid rescue during the first 24 h in the dexmedetomidine groups [27,28].

Subarachnoid hemorrhage

Subarachnoid hemorrhage is among the most challenging conditions that neurointensivists manage and the associated headaches that patients report complicates their treatment even further. According to one retrospective review of Hunt and Hess 1–3 patients, 73% of patients experience severe headache up to 2 weeks from onset. Of the 77 patients reviewed, 51 were aneurysmal (44 secured by endovascular route, five by craniotomy, and two unsecured). The most commonly prescribed analgesics were acetaminophen, dexamethasone, and an assortment of opioids [29]. Similarly, another recent cohort study showed that 89% of the 46 included patients had a severe headache during their hospitalization for subarachnoid hemorrhage. All patients received acetaminophen, whereas 43 received opioids with a mean morphine equivalent dose of 15.7 mg/day [30]. These findings are consistent with the frequency of severe headache (75%) reported in an older study of nonaneurysmal subarachnoid hemorrhage. Interestingly, follow-up demonstrated persistent headache in 25% of patients after 2 or more years [31]. As with postoperative craniotomy patients, pain in the acute subarachnoid hemorrhage population continues to be a significant issue that calls for novel approaches and research.

SPINE PAIN

The most common causes for back pain include discogenic disease and ligamental hypertrophy leading to nerve root or cord compression [32]. According to a recent estimate, 16–33% of patients require chronic opioid therapy before back surgery [33]. The combination of opioid dependence, preexisting somatic, and neuropathic pain and acute postsurgical pain poses a substantial therapeutic challenge. This section will focus on updated literature on multimodal treatment of spinal pain including postoperative pain and posttraumatic neuropathy.

Acetaminophen

Given its tolerability, safety profile, and low cost, oral acetaminophen has historically been a common component of multimodal pain management...
strategies. i.v. acetaminophen was introduced to the United States in 2010 and there has been some interest in its use for postoperative pain especially in cases where nausea and vomiting limit oral administration of pain medications. It has also been proposed that increased acetaminophen concentrations in the cerebrospinal fluid when administered i.v. may provide some advantages over the oral formulation [34]. In a retrospective review of spine surgery patients who received i.v. vs. oral acetaminophen, the i.v. route was associated with lower opioid consumption as well as improvements in other healthcare quality metrics (Table 2) [35]. Unfortunately, the high cost of the i.v. formulation

Table 2. Summary of nonopioid trials in spine pain

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population (N)</th>
<th>Intervention</th>
<th>Findings</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Naik et al. [32]**/</td>
<td>Patients undergoing &gt;three levels of thoracic and/or lumbar spine surgery (131)</td>
<td>Loading dose of 1 mcg/kg (IBW) dexmedetomidine intravenously followed by a continuous infusion of 0.5 mcg/kg/h (IBW) vs. placebo</td>
<td>Dexmedetomidine was not associated with reduced postoperative opioid use or better pain scores up to 3 days after spine surgery. The study was terminated early because of limited power to demonstrate a significant reduction in opioid use.</td>
<td>A potential reason for the lack of a long-term effect of dexmedetomidine in this study was the use of methadone (0.2 mg/kg [ideal body weight]), for intraoperative analgesia.</td>
</tr>
<tr>
<td>Hansen et al. [33]**/</td>
<td>Spine surgery patients (112 586)</td>
<td>Forty-six percentage had received i.v. APAP vs. 80% of the i.v. APAP group received i.v. APAP on the day of surgery, only 16% received i.v. APAP on the first postoperative day. Twenty percentage of the oral APAP group used oral APAP on the day of surgery, and 33% received oral APAP on the first postoperative day.</td>
<td>Based on adjusted models, i.v. APAP was associated with 0.68 days shorter length of stay (P &lt; .001) and 13 mg lower average daily morphine equivalent dose (P &lt; .0001)</td>
<td>Given the retrospective nature of this trial, the results should be interpreted with caution as confounders such as differences in regional anesthesia techniques or other analgesic medications may have played a role</td>
</tr>
<tr>
<td>Vagh et al. [36]**/</td>
<td>Patients undergoing laminectomy (114)</td>
<td>600 mg gabapentin 2 h before surgery and 300 mg after surgery vs. 400 mg celecoxib 2 h before surgery and 200 mg 6 h after surgery vs. placebo</td>
<td>Mean pain severity score in the gabapentin group was less than placebo and celecoxib groups at different intervals (P &lt; .001) Mean morphine doses were 11.9, 22.8, and 30.1 mg in the gabapentin, celecoxib, and placebo groups, respectively (P &lt; .001)</td>
<td>All patients were induced with thiopentone (5 mg/kg i.v.), atracurium (0.5 mg/kg i.v.), and maintained with isoflurane (1–1.5%) and nitrous oxide (50%) in oxygen. Fentanyl i.v. was given during the procedure per clinical discretion</td>
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<tr>
<td>Fujita et al. [37]**/</td>
<td>Lumbar interbody fusion surgery (97)</td>
<td>Diazepam 5 mg as an active placebo, pregabalin 75 mg, or pregabalin 150 mg were orally administered 2 h prior to surgery based on patient randomization</td>
<td>Patients who received pregabalin (150 mg) 2 h before surgery had lower pain scores. i.v. Morphine use with patient-controlled analgesia was less during 48 h postsurgical period 150 mg group.</td>
<td>Only VAS scores for resting pain during mobilization and rest 150 mg were higher in the placebo group.</td>
</tr>
<tr>
<td>Dong et al. [38]**/</td>
<td>Spinal surgery patients (23)</td>
<td>Dose of dexmedetomidine was determined using the modified Dixon’s up-and-down method (0.5 mcg/kg as a step size), low dose sufentanil (3.0 mcg/kg in 250 ml) at 4 ml/h was given to all patients</td>
<td>Optimal dose of dexmedetomidine was 4.33 mcg/kg when given with low dose continuous infusion of sufentanil</td>
<td>Preoperative low dose infusion of sufentanil might have influenced pain intensity in the early postoperative phase</td>
</tr>
<tr>
<td>Nielsen et al. [39]**/</td>
<td>Spine surgery patients (110)</td>
<td>Pain during mobilization and rest 2 h after intervention were not different and no significant difference in total i.v. morphine use was noted 0–4 h</td>
<td>Single dose of chlorozoxazone 500 mg was used in this study. Commonly prescribed regimens are 250–500 mg TID. Studies with higher doses preoperatively may provide additional information regarding its analgesic effects in acute postsurgical pain</td>
<td>Pain during mobilization and rest 2 h after intervention were not different and no significant difference in total i.v. morphine use was noted 0–4 h</td>
</tr>
<tr>
<td>Garg et al. [40]**/</td>
<td>Spine surgery patients (66)</td>
<td>Group K: ketamine bolus followed by infusion of 0.25 mg/kg/h along with midazolam bolus 10 mcg/kg and infusion at 10 mcg/kg/h Group D: dexmedetomidine bolus 0.5 mcg/kg followed by 0.3 mcg/kg/h infusion Group C: Placebo</td>
<td>Mean pain-free time in group K (860 min) and group D (580 min) were longer than group C (265 min) (P &lt; .002) Ketamine reduced morphine requirement by 74%, whereas dexmedetomidine decreased it by 54%</td>
<td>Pain during mobilization and rest 2 h after intervention were not different and no significant difference in total i.v. morphine use was noted 0–4 h</td>
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APAP, acetaminophen; IBW, ideal body weight; PCA, patient-controlled analgesia.
of acetaminophen limits its availability in many institutions at this time.

**Gabapentinoids**
Gabapentin, originally classified as an anticonvulsant agent, has become useful in treating neuropathic pain [41]. More recently, a randomized double-blinded trial that compared the effects of gabapentin and celecoxib on pain and complications after elective laminectomy concluded that the gabapentin group had lower pain intensity measured by VAS and reduced morphine consumption over controls (Table 2) [36**].

Pregabalin is structurally related to gabapentin but its analgesic effects on postoperative pain have not been well evaluated. A single center prospective double-blinded randomized trial recently assessed the dose-related effects of pregabalin on postoperative pain intensity and morphine use in elective posterior lumbar interbody fusion surgery. High-dose pregabalin (150 mg) when given 2 h before surgery was associated with lower VAS up to 48 h after surgery. i.v. morphine use by PCA was also lower during this time (Table 2) [37**].

Many patients with spinal cord injury suffer from neuropathic pain. Although pregabalin’s use for neuropathy is not a novel intervention, as it is Food and Drug Administration approved for this indication, its effect in combination therapy with other analgesics was only recently evaluated [42]. Data were derived from two randomized placebo-controlled trials for the treatment of neuropathy because of spinal cord injury and seven trials for the treatment of postherpetic neuralgia. Results of the spinal cord injury trials demonstrated that pregabalin (150–600 mg) improved pain compared to placebo up to 12 weeks in both groups receiving concomitant neuropathic pain medications and those not receiving other neuropathic pain medications. Pain scores were not substantially improved in patients receiving other neuropathic pain medications. This analysis was limited in that the original trials of pregabalin were not sufficiently powered to assess the effects of concomitant neuropathy medications.

**Dexmedetomidine**
Dexmedetomidine, an alpha 2 agonist, used for sedation has known analgesic and opioid-sparing effects [43]. Most published studies have focused on lumbar laminectomy patients [44,45]. More recently, the analgesic role of intraoperative dexmedetomidine was studied in patients undergoing more complicated spine surgeries such as multilevel deformity correction. Although not sufficiently powered, this study failed to show intraoperative dexmedetomidine is associated with reduced postoperative opioid use or improved pain scores for up to 3 days (Table 2) [32**]. Another recent study aimed to determine the optimal dose of dexmedetomidine in addition to sufentanil to provide optimal pain control in spinal surgery patients. Optimal dose of dexmedetomidine was concluded to be a mixture of 4.33 mcg/kg combined with 3.0 mcg/kg of sufentanil in 250 ml with a continuous infusion of 4 ml/h for satisfactory pain control after spine surgery (Table 2) [38**].

**Chlorzoxazone**
Chlorzoxazone, a centrally acting muscle relaxant, is commonly used to relieve back pain and muscle stiffness. A previous Cochrane review concluded that muscle relaxants may be effective as short-term treatment of acute back pain [46]. More recently, the analgesic effects of chlorzoxazone on acute pain after spine surgery were studied in a single-center, prospective, randomized, blinded trial. Authors concluded that chlorzoxazone did not reduce acute postoperative pain in patients with moderate-to-severe pain and therefore cannot be recommended (Table 2) [39**].

**Ketamine**
Ketamine, an NDMA receptor antagonist, is an effective analgesic [47]. In a recent trial, low dose ketamine was compared with low dose dexmedetomidine after spine surgery. Patients in the ketamine group reported lower pain scores and reduced morphine requirements (Table 2) [40**].

**Intrathecal morphine**
The efficacy of a single dose of intrathecal morphine intraoperatively vs. epidural hydromorphone for postoperative analgesia after posterior spinal fusion was studied in adolescents with idiopathic scoliosis. Intrathecal morphine in addition to nonopioids improved the transition to oral analgesics as well as early ambulation and discharge (Table 3).

**Patient-controlled epidural analgesia**
Patient-controlled epidural analgesia (PCEA) and i.v. PCA, are effective interventions to treat postoperative pain. Although controversial, increasing evidence is revealing that PCEA is more effective than i.v. PCA after spinal fusion surgery presumably because of the longer duration of epidural
analgesia and lower dosages required to manage pain [50,51]. A recent trial compared the effects of sufentanil i.v. PCA vs. sufentanil and ropivacaine PCEA. Significantly lower VAS scores in the PCEA group up to 2 days were observed but at 72 h, the VAS scores between groups became comparable (Table 3) [49**].

**CONCLUSION**

As the trend toward opioid sparing analgesic strategies continues, the dearth of treatment options for the pain experienced by patients with acute neurological conditions becomes more apparent. Meanwhile, growing concerns over opioid addiction are compelling clinicians to limit the use of opioids even further. Yet inadequate pain control is no longer tolerated in the modern era of patient-satisfaction focused health care. Although pain has been recognized to cause a systemic stress response and neurovascular effects that may harm patients recovering from neurologic illnesses, ultimately, the transition from acute to chronic pain and disability caused by inadequate pain control is what may settle the pain controversy once and for all. Additional investigations into the link between acute and chronic pain, particularly in the neurocritical care literature, are in critical shortage.
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17. Study that demonstrated reduced pain scores in craniofacial surgery patients who received local anesthetic scalp blockade.


19. Study that demonstrated improved analgesia following administration of scalp block in infratentorial craniotomy patients.


22. Study that demonstrated improved analgesia following administration of scalp block in infratentorial craniotomy patients.

23. Intraoperative dexmedetomidine reduced postoperative pain and opioid consumption.


25. In a retrospective review, i.v. acetaminophen was associated with lower opioid consumption as well as improvements in other healthcare quality metrics when compared to oral acetaminophen.


27. Use of dexmedetomidine during spine surgery did not improve analgesia, likely because of an underpowered study.

28. In a retrospective review, i.v. acetaminophen was associated with lower opioid consumption as well as improvements in other healthcare quality metrics when compared to oral acetaminophen.

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31. Study demonstrating improved analgesia and reduced opioid consumption following spine surgery in patients treated with pregabalin.

32. Optimal dose of dexmedetomidine was evaluated in patients undergoing spine surgery.

33. The muscle relaxant chlorozone was not effective in improving analgesia following spine surgery.

34. In a retrospective review, i.v. acetaminophen was associated with lower opioid consumption as well as improvements in other healthcare quality metrics when compared to oral acetaminophen.

35. Use of dexmedetomidine during spine surgery did not improve analgesia, likely because of an underpowered study.


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52. In a retrospective review, i.v. acetaminophen was associated with lower opioid consumption as well as improvements in other healthcare quality metrics when compared to oral acetaminophen.
