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Peri-Operative Pain Control in the Neurosurgical Patient

M. Neil Woodall, Nathan D. Todnem, Joseph Withrow BS and Scott Y. Rahimi*

Department of Neurological Surgery, Georgia Regents University Augusta, Georgia, USA

***Corresponding authors:** Scott Y. Rahimi, MD, Department of Neurological Surgery, Georgia Regents University Augusta, Georgia, USA, E-mail: SRAHIMI@augusta.edu

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Abstract

The importance of peri-operative pain control cannot be overstated. The overwhelming majority (87%) of patients experience pain after craniotomy – 44% of patients report moderate pain and 10% report severe pain in the first 24 hours post-procedure. Adequate analgesia in the post-operative period is associated with improved patient satisfaction, increased mobility, early ambulation, shorter hospital stays, and reduced cost. There has been a tendency in neurosurgery to underestimate the severity of, and therefore under-treat, post-operative pain following craniotomy and spinal surgery. An increasing body of evidence suggests that aggressive pain control in the acute post-operative period may reduce the risk of chronic pain and chronic opioid dependence. Analgesic options are limited by bleeding risk, the need for a reliable neurologic examination, and the risk for pseudoarthrosis following spinal fusion. Prevention of acute severe pain is likely to improve visual analog scale (VAS) scores in the hospital, reduce opioid consumption, reduce opioid related side effects, and decrease the likelihood of going on to develop chronic pain. We would recommend a multi-modal strategy including the liberal use of opioids coupled with acetaminophen, gabapentin/pregabalin, and non-narcotic analgesics such as tramadol and COX-2 inhibitors. While the liberal use of opioids in encouraged in the early post-operative period, patients must be discharged with a clear and concise weaning schedule. The use of local anesthetic is recommended also. Pre-treatment protocols and the use of epidural catheters represent therapeutic options that warrant further study. More study is required both in the laboratory and in the clinic to enhance our understanding of the pain phenomenon and to formulate better treatment.

Keywords: Craniotomy; Spine surgery; Neurosurgery; Post-operative pain; Peri-operative pain; Opioid; Multimodal pain management

Core Tip

The overwhelming majority (87%) of patients experience pain after craniotomy – 44% of patients report moderate pain and 10% report severe pain in the first 24 hours post-procedure. There has been a tendency in neurosurgery to underestimate the severity of, and therefore under-treat, post-operative pain following craniotomy and spinal surgery. An increasing body of evidence suggests that aggressive pain control in the acute post-operative period may reduce the risk of chronic pain and chronic opioid dependence. We would recommend a multi-modal strategy including the liberal use of opioids coupled with acetaminophen, gabapentin/pregabalin, and non-narcotic analgesics such as tramadol and COX-2 inhibitors.

This study was conducted with the approval of the Georgia Regents University Institutional Review Board. The authors have no financial disclosures or conflicts of interest to report.

Introduction

The importance of peri-operative pain control cannot be overstated. The overwhelming majority (87%) of patients experience pain after craniotomy – 44% of patients report moderate pain and 10% report severe pain in the first 24 hours post-procedure [1]. Adequate analgesia in the post-operative period is associated with improved patient satisfaction, increased mobility, early ambulation, shorter hospital stays, and reduced cost [2,3]. There has been a tendency in neurosurgery to underestimate the severity of, and therefore under-treat, post-operative pain following craniotomy [4]. An increasing body of evidence suggests that aggressive pain control in the acute post-operative period may reduce the risk of chronic pain and chronic opioid dependence [5-7].

Limitations

Neurosurgery patients represent a complex and heterogenous patient population. Procedures range from supratentorial burr holes to multi-level thoracolumbar deformity correction. Acute perioperative pain control is challenging in these patients because of restrictions imposed by the nature of the disease processes and procedures. There is a tendency to limit narcotics in cranial patients for fear of masking the neurologic examination, and for fear of hypercapnea that might lead to cerebral vasodilation and subsequent increases in intracranial pressure [8]. For both cranial and spine patients, there is hesitation regarding the use of agents that could inhibit platelet aggregation such as non-steroidal anti-inflammatory drugs (NSAIDs) because of the risk of post-operative epidural hematoma, resulting in neurologic deficit and an unplanned return to the operating room [9]. Some spine surgeons avoid NSAIDs because animal studies have suggested that they may interfere with bone healing [10]. Epidural infusions can be problematic because of a high incidence of numbness and tingling masking the neurologic examination [11]. Furthermore, the intraoperative anesthetic technique is sometimes limited by a need for neuro-monitoring (motor evoked potentials, somatosensory evoked potentials, and electromyography), avoidance of certain inhalational anesthetics, need for a rapid wake-up and neurological examination, and sometimes by the need for awake-craniotomy for functional mapping [12].

Importance of pain control

Despite these limitations, adequate peri-operative analgesia is mandatory for neurosurgery patients. Improved pain control as expressed by improved visual analog scale (VAS) scores correlate with improvements in patient anxiety, fear, and ability to rest [8]. Pain and gastrointestinal dysfunction are the leading causes of delayed in-hospital recovery after spine fusions [13]. Improved pain control is associated with deep breathing as well as early ambulation which, theoretically, reduce the risk of pneumonia, deep vein thrombosis, and pulmonary embolism [2,3,8]. Adequate analgesia results in decreased sympathetic outflow, autonomic stability, and improved blood pressure – arterial hypertension is a risk factor for post-operative intracranial hematoma [1]. Excellent pain control should improve patient comfort, prevent hospital-associated complications, shorten length of stay, and reduce cost.

Who is at risk?

Women, younger patients, and patients on chronic preoperative opioid therapy tend to report higher post-operative pain levels following craniotomy [14]. The likelihood of experiencing post-operative pain following craniotomy decreases by 3% for each additional year of life [1]. Historically, infratentorial operations were thought to be more painful than supratentorial operations. More recent evidence suggests that craniotomies that traverse the temporal or cervical musculature tend to be the most painful – muscle dissection seems to produce the majority of acute craniotomy pain [1]. Not surprisingly, patients undergoing spinal surgery tend to experience more post-operative pain than after craniotomy. Spine surgery patients tend to have higher pre-operative VAS scores than craniotomy patients, and their pain shifts from referred (radicular) pain pre-operatively to local (incisional) pain post-operatively [4]. Patients with pre-operative pain experience more post-operative pain than those without pain prior to surgery [4]. Patients on chronic opioid therapy prior to surgery have increased post-operative opioid requirements, more severe post-operative pain, slower pain resolution, and have a decreased incidence of post-operative freedom from opioids [15,16]. In one study, 59% of patients using pre-operative opioids were still using them 1 year after surgery [16]. Psychiatric comorbidities may also play a role in the pathophysiology of chronic post-operative pain syndromes. Flexman et al. noted an association between the presence of anxiety and depression and the development of chronic post-craniotomy headache [14]. A large retrospective study of patients undergoing transphenoidal surgery found that patients who developed diabetes insipidus had higher narcotic requirements in the recovery room [17]. They postulate that certain emotional states can interrupt ADH production, and that pain is one such state [18]. These findings underscore the complexity of pain pathways and their integration into other neural systems.

Pain begets pain

Aggressive pain control improves patient comfort in the acute peri-operative period, but may also decrease the likelihood of going on to develop chronic pain [5-7,19-21]. Acute severe pain may sensitize pain pathways both centrally and in the periphery. Nociceptive nerve endings in the periphery (A-delta and C fibers) may become sensitized, firing at lower thresholds in the setting of tissue damage and inflammation under the influence of cyclooxygenase-2 (COX-2) and interleukin 1-beta (IL-1B) [5-7]. Centrally, second order spinal neurons are sensitized via activation of N-methy-D-aspartate (NMDA) channels and changes in neuronal cytoarchitecture. The sensitization of second order neurons has been implicated in hyperalgesia and neuropathic pain [5,7]. On this basis, authors have suggested strategies to avoid peripheral and central sensitization to pain. These strategies include the use of local anesthetics, neuraxial blockade, analgesic pre-treatment, and the use of non-narcotic adjunctive treatments such as gabapentin and pregabalin [5-7,14,19].

Plan of attack

We have established that pain control is an important issue for patients undergoing neurosurgical procedures, and have highlighted some of the limitations in this patient population. It is clear that keeping pain under tight control throughout the peri-operative period will reduce narcotic requirements, improve VAS scores, and reduce the likelihood of developing chronic pain. We will now discuss strategies for managing peri-operative pain in the neurosurgical patient including the role for local anesthetics, pre-medication, a multi-modal approach to pain management, and the role for epidural catheters following spine surgery.

Local anesthetic

Local anesthesia has a rich history in neurosurgery. Some of the earliest neurosurgical procedures were carried out under scalp block with local anesthesia before general anesthesia was safe and reliable. Craniotomy is still sometimes performed under scalp block when the patient must be awake for speech or motor mapping, or as is sometimes necessary for deep brain stimulator electrode placement. A scalp block requires blockade of the supratrochlear, supraorbital, zygomaticotemporal, posterior branch of great auricular, lesser occipital, greater occipital, and third occipital nerves [12]. Scalp blockade does not anesthetize the dura, but local anesthetic can be injected into the dura using a tuberculin syringe. Use of local anesthetic minimizes the hemodynamic response to surgical pain, reduces anesthetic requirements, and may reduce post-operative narcotic requirements [12]. While the use of local anesthesia during craniotomy does not consistently lower VAS scores, it seems to dramatically reduce the incidence of chronic post-craniotomy headache and chronic post-operative pain [14,19]. It is possible that the use of local anesthetic prevents the sensitization of peripheral nociceptive fibers, as discussed previously.

Pre-medication

A number of investigators have used pre-medication as a strategy to improve post-operative pain control and reduce the risk of developing chronic pain. Pre-emptive protocols generally involve the administration of non-narcotic analgesics such as acetaminophen, NSAIDs, or gabapentin alone or in combination for 2 weeks to 1-2 hours prior to surgery [22]. The goal of this strategy is to inhibit nociceptive input at the time of surgery and blunt the pain response. Theoretically, pre-medication could prevent the CNS plasticity that is thought to occur in response to painful stimuli [23]. A recent meta-analysis found fair evidence that pre-medication improves post-operative pain control [22]. Low doses of analgesics may be required pre-operatively to prevent central sensitization, while high doses might be required post-operatively once sensitization has occurred [23]. Gabapentin 1200 mg given 1 hour before spine surgery has been shown to decrease pain scores at 1, 2 and 3 hours. The patients pre-medicated with gabapentin required less total morphine, had lower

rates of vomiting and urinary retention, and no difference in adverse events post-operatively [24].

A Multi-modal approach

The rational for a multi-modal approach to pain management involves using multiple agents with varying mechanisms of action to target pain pathways at multiple sites. The goal is synergism allowing for improved efficacy, reduction in dose of each agent, and improvement in toxicity and side effects. A recent literature review by Devin et al. found Level I evidence to support the use of gabapentin, acetaminophen, neuraxial blockade, and long-acting local anesthetics; Level II evidence to support the use of NSAIDs; and conflicting evidence regarding the use of ketamine and muscle relaxants [22].

Opioids

Historically craniotomy pain was underestimated, and there was a tendency to avoid opioids due to their sedating properties [8]. Currently, however, pain after craniotomy is managed with acetaminophen and opioids on an as needed (PRN) basis in most centers in the United States [25]. Options include readily available PRN opioids (as in an ICU setting), scheduled opioids, or IV PCA pumps. There is some evidence to suggest that PCA dosing is a more effective option than PRN administration of opioids following craniotomy [14].

Anti-convulsants

Gabapentin and pregabalin have both been shown to reduce pain and opioid requirements post-operatively [22]. Gabapentin has been shown to decrease morphine consumption in the recovery room, on post-op day (POD1) and POD2 in pediatric patients undergoing spinal fusion. Gabapentin also decreased pain scores in recovery and the morning after surgery [5]. Gabapentin was also shown to be effective at reducing pain scores and opioid requirements as part of a pre-medication protocol for spine surgery patients [24]. Other authors have postulated that gabapentin may have a role in the prevention of chronic post-craniotomy headache via inhibition of pain pathway sensitization [14]. Pregabalin has also been shown to improve post-operative pain scores, particularly in patients with neuropathic pain. Reports of respiratory depression associated with pregabalin has prompted investigators to identify relative contraindications for the peri-operative use of pregabalin which include sleep deprivation, concomitant use of neuraxial opioids, sleep apnea, renal insufficiency, and old age. Pregabalin must be used with caution or avoided in these patients [26].

Acetaminophen

Oral acetaminophen has been a mainstay of post-operative analgesia in neurosurgery for some time [25]. In the orthopedic surgery population, acetaminophen has been shown to improve pain scores post-operatively but has not been shown to decrease opioid requirements [22]. More recently, intravenous (IV) acetaminophen formulations have been introduced for peri-operative analgesia. A prospective randomized controlled trial conducted at our institution has shown decreased VAS scores in the first 24 hours, decreased opioid requirements, and a trend toward decreased length of stay in the IV acetaminophen group when compared to controls (Rahimi and Woodall, unpublished data).

NSAIDs

NSAIDs have been shown to reduce VAS scores and reduce opioid requirements by 20-30% in some studies [22,27]. NSAIDs include non-selective COX inhibitors such as ketorolac, indomethacin, flurbiprofen, lornoxica, and piroxicam as well as COX-2 inhibitors such as celecoxib, refecoxib, and parecoxib [27]. NSAIDs are used with caution in the cranial population because of concerns of inhibition of platelet aggregation and subsequent risk of post-operative hematoma [9]. NSAIDs are used with caution in the spine population because of concerns about inhibition of bone healing and a theoretical reduction in fusion rates [10]. Despite these concerns, half of neurosurgical units in the United States routinely prescribe NSAIDs [14]. There is level II evidence that short term use of NSAIDs does not cause an appreciable reduction in fusion rates following spinal arthrodesis [22].

COX-2 Inhibitors

Paracoxib has been shown to reduce morphine consumption by 39% and VAS scores by 30% without additional side effects in a randomized controlled trial [28]. A prospective study conducted at our institution found that the addition of COX-2 inhibitors provided improved pain control, decreased opioid dosage and side effects, encouraged earlier ambulation, and decreased hospital costs [2]. COX-2 inhibitors should be avoided in patients with renal disease, coronary artery disease, and cerebrovascular disease [22].

Tramadol

Although some authors consider tramadol to be a third or fourth line agent, it has been shown to be a useful adjunct in the control of post-operative pain in craniotomy patients [14]. In a randomized controlled trial conducted at our institution, the addition of tramadol to the post-operative pain protocol resulted in significant improvements in length of stay, VAS scores, and opioid consumption [3].

Ketamine

Historically, ketamine has been avoided in neurosurgical patients because of concerns about increased intracranial pressure and increased cerebral blood volume [29,30]. A flurry of recent literature has focused on the safety of ketamine with regard to intracranial pressure [29-33] and there has been renewed interest in the use of ketamine infusions in patients undergoing spine surgery. Investigators have demonstrated improved VAS scores with IV ketamine infusions in spine surgery patients [34-36]. Data is mixed regarding the effect of ketamine on opioid consumption in the post-operative period. There were no significant adverse events reported with the use of ketamine after spine surgery in any of the cited studies [34-38].

Neuraxial blockade

The route of drug delivery influences dose requirement and systemic side effects. Intrathecal injections, intrathecal infusions, and epidural infusions have been shown to reduce post-operative pain and post-operative narcotic requirements in spine surgery patients [22]. Techniques generally involve placement of an epidural catheter at the time of surgery via a Touhy needle inserted through the paramedian soft tissues. Catheter placement can optionally be confirmed via radiography or fluoroscopy with trans-catheter injection of radio-opaque contrast medium [39]. Investigators using epidural infusions of

opioids alone or in combination with local anesthetics have achieved earlier return of bowel sounds [13], earlier oral intake [40], significant reduction in opioid requirements [41], reduced need for muscle relaxants [42], reduction in VAS at 12, 24, and 48 hours [43], and improved patient satisfaction compared to controls [44]. The use of epidural catheters does not seem to be associated with an increased risk of infection or opioid-related symptoms. There was, however, a 41% incidence of post-operative lower extremity parasthesias in comparison to placebo in one study [11]. Clouding of the neurologic examination represents a potential drawback to post-operative epidural infusions.

Conclusions

Pain in the post-operative neurosurgical patient is an under-appreciated and under-treated problem. Neurosurgical patients represent a heterogeneous group of both cranial and spine patients. Analgesic options are limited by bleeding risk, the need for a reliable neurologic examination, and the risk for pseudoarthrosis following spinal fusion. Prevention of acute severe pain is likely to improve VAS scores in the hospital, reduce opioid consumption, reduce opioid related side effects, and decrease the likelihood of going on to develop chronic pain. We would recommend a multi-modal strategy including the liberal use of opioids coupled with acetaminophen, gabapentin/pregabalin, and non-narcotic analgesics such as tramadol and COX-2 inhibitors. While the liberal use of opioids is encouraged in the early post-operative period, patients must be discharged with a clear and concise weaning schedule to prevent rebound pain and persistent pain that could necessitate chronic opioid therapy. The use of local anesthetic is recommended. Pre-treatment protocols and the use of epidural catheters represent therapeutic options that warrant further study. More study is required both in the laboratory and in the clinics to enhance our understanding of the pain phenomenon and to formulate better treatment.

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