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Multimodal Analgesia in Spine Surgery: A Commentary

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Abstract

Chronic back pain is a multifactorial issue requiring a concerted effort amongst members of the multidisciplinary team throughout a patient's surgical course to provide the best environment for targeted therapy in order to reduce postoperative morbidity. Implementing a program designed to reduce opioid consumption and provide adequate pain control requires a commitment to a multidimensional approach involving multimodal anesthetic/analgesia (MMA) and functional restoration by all members of the multidisciplinary team. Postoperative pain involves several pathways including nociceptive, neuropathic and inflammatory pain responses. Current literature focuses on the role of neuroplasticity in pain and injury as well as management protocols designed to target several pain pathways. Using a combination of medications administered pre-, peri- and postoperatively provides the basis for multimodal analgesia (MMA) protocols, which have demonstrated more effective pain control than a single standard therapeutic measure. The preferred pain management technique is a controversial topic in orthopedic specialties, including spine surgery. However, based on current literature, a successful minimally invasive spine surgery program involves a multidisciplinary team combining several pain management therapies into multimodal analgesia resulting in the successful control of postsurgical pain

Keywords: Multimodal analgesia; MMA; Spinal surgery; Minimally invasive spinal surgery; Patient controlled analgesia; PCA; Postoperative pain

Introduction

Chronic back pain is a multifactorial issue, resulting in a reduction in physical, emotional, psychological, and social function [1]. The primary treatment emphasizes an individualized, nonoperative pain management plan focused on education and counseling, improved muscular stability achieved through physical therapy and home exercise, as well as non-surgical interventions, over the counter, and prescription medication regimens [2,3]. Once conservative management fails, definitive surgical treatment is considered. Traditional open procedures involve large exposures, extensive soft tissue dissection and retraction leading to significant peri- and postoperative morbidity [4]. Technological advancements allowed a shift in surgical paradigms towards minimally invasive surgery (MIS) leading to a decline in peri- and postoperative morbidity. Smaller incisions and reductions in approach-related soft tissue damage associated with MIS techniques led to decreased operative times and blood loss, shorter length of hospital stay, and a faster recovery and return to work [4,5]. However, one of the most significant benefits associated with MIS is the improvement in postoperative pain and narcotic utilization compared to the open procedures [4].

Although patients experience reduced pain and narcotic consumption with MIS spinal procedures, a residual level of postoperative discomfort and opiod consumption will persist following surgery, contributing to delays in mobilization and rehabilitation [6]. Therefore, a concerted effort amongst members of the multidisciplinary team throughout a patient's surgical course will provide the best environment for targeted therapy to reduce postoperative morbidity. Implementing a program such as this requires a commitment to a multidimensional approach involving multimodal anesthetic/analgesia (MMA) and functional restoration by all members of the multidisciplinary team.

One successful application of this philosophy is a protocol described by Berger, et al. [7] for MIS outpatient joint replacements. Prior to their operation, patients must attend a class taught by the nursing staff, which aims to address preoperative expectations, hospital course and postoperative care. Perioperatively, patients receive multiple narcotic medications, IV fluids, epidural anesthesia and analgesia, and anti-emetics to provide adequate pain relief while minimizing morbidities such as nausea, vomiting and hypotension [8]. Additionally, a clinical nurse would be present postoperatively to quickly address any complications and ensure sufficient pain control. Aside from immediate medical care, rehabilitation goals and timelines are a critical portion of the comprehensive plan. Patients are instructed to attend a physical therapy session covering proper techniques for weight bearing and ambulation with crutches, and are encouraged to walk independently the day of surgery [7]. Using this protocol, all 150 patients included in the analysis were discharged home the day of surgery and able to walk independently or with minimal aid [7]. Given the success in total joint replacement procedures, these methods should be adapted for use in MIS spine surgery.

Given the challenges presented with MIS spine surgery, anesthesiologists hold a critical role in the successful implementation of a multidisciplinary plan. With the increasing popularity of MIS surgery, same or next day discharge has become expected for many elective procedures. This requires that all aspects of anesthesia and analgesia be optimized for quick recovery without sacrificing patient comfort [9]. Uncontrolled pain, postoperative nausea and vomiting, transient impairment of psychomotor skills, and impaired bowel and bladder function are all anesthetic and analgesic side effects that must be controlled to prevent delayed discharge [10].

Postoperative pain involves nociceptive, neuropathic and inflammatory pain responses directly proportional to the number of vertebral levels involved in the operation, irrespective of the vertebral

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region involved (cervical, thoracic, or lumbar) [11]. Several of the biochemical pathways that contribute to postoperative pain originate with the surgical incision. The most targeted of these pathways for therapeutic benefit is the inflammatory response [12]. Cellular damage resulting from injury, such as the surgical incision, leads to the activation of the inflammatory response resulting in local effects on the biochemical and pathophysiologic pathways of inflammation, edema, pain and fever [12,13]. Local prostaglandin induced activation of nociceptors results in the peripheral sensitization of the nervous system, leading to the acute pain response, known as primary hyperalgesia [14,15].

Several studies have examined the predominant prostaglandins and cytokines involved in the acute pain response, determining prostaglandin E2 (PGE2) and interleukin-6 (IL-6) as the principal mediators of inflammation and the associated pain [12,15,16]. Following total hip arthoplasty, Buvanendran, et al. [12] has demonstrated increases in the peripheral and local concentrations of PGE2, IL-6, IL-8, and IL-1β as well as IL-6 concentration in the cerebrospinal fluid (CSF) within the first 30 hours postoperatively. Locally stimulated by TNF-α, the initial release of IL-6 from endothelial and epithelial cells, fibroblasts and monocytes can be quantified with the concentration correlating to inflammation severity [15,16]. The authors noted the magnitude of the IL-6 response varied by surgical procedure, with a maximal increase in concentration on postoperative day one, preceding the rise in plasma neutrophil elastase (NE), and the acute phase reactants, C-reactive protein (CRP) and pancreatic secretory trypsin inhibitor (PSTI) [15,16]. Similarly, the concentration of serum IL-6 was correlated with duration of surgery, volume of blood loss and complication rate [15].

Overtime, prolonged nerve impulse and interleukin stimulation on the central nervous system results in the activation of N-Methyl D-aspartate (NMDA) receptors known as central sensitization or secondary hyperalgesia [12,13]. The resultant modification in production of COX and nitric oxide synthase (NOS) leads to the up-regulation of prostaglandin synthesis and subsequent neuronal remodeling, known as neuroplasticity and long-term potentiation leading to chronic pain [13].

The concept of neural reorganization, or neuroplasticity, is the ability of neurons to adapt to altered afferent responses in composition, organization, and functional role. It has been implicated in multiple different contexts with notable benefits demonstrated in cognitive ability and learning; however, there has been an increasing focus on the role of neuroplasticity in pain and injury. Initially, the rapid adaptation of neurons provides assistance in the bodies response to pain, limiting the damaged structures from continued irritation. However, overtime, continued stimulation induces both structural and chemical changes at the neural synapse that results in altered pain sensation and response control, amplifying afferent pain signals experienced by the patient [17-21]. It has been hypothesized that alterations to the pain pathway caused by the initial insult and subsequent inflammation leads to chronic pain through reactivation, continued reinforcement, and maintenance of the altered pathways [22,23]. This form of associative learning among neurons in the central nervous system is believed to be only one factor contributing to chronic pain. Fortunately, several of these changes have demonstrated reversibility. Patients undergoing total hip arthroplasty for osteoarthritis experience decreases in the volume of gray matter that is successfully reversed with an associated decrease in pain following surgery [17,24]. Similar properties have been demonstrated in post-amputation patients in which the areas of the primary sensory and motor cortices corresponding to the amputated limb are recruited by adjacent neurons to contribute to the function of different muscle groups. Neuroplasticity, therefore, likely contributes to spine surgery patient's chronic pain and emphasizes the necessity to not only focus on the physical and structural pathology but also target neuronal remodeling in order to effectively treat chronic pain conditions.

In addition to the chronicity of pain and neuroplasticity making postoperative pain management more complicated, current evidence suggests the majority of patients undergoing spinal procedures have used long-term over-the-counter analgesic and prescription narcotic medications to manage their chronic pain. Chronic use of these medications leads to an altered perception of pain and reduced response to common medications [11]. Therefore, a protocol aimed at reducing narcotic consumption and focusing on the variety of pain mechanisms is necessary to adequately manage this patient population's postoperative pain [6,25].

Inflammatory and nociceptive pain associated with surgical procedures is often localized, transient, and generally shows improvements over time, making it a good candidate for medical therapy. Several studies have demonstrated the benefit of preemptive analgesia in reducing this pain. As Kim, et al. [26] stated, preemptive analgesia is based on the concept of central sensitization. The author states the goal is to inhibit the activation of hyperactive second order neurons in the dorsal horn that have been sensitized and respond to inappropriate stimuli. By providing pharmacologic intervention to inhibit inflammatory and nociceptive pathways prior to surgery, preemptive analgesia has been associated with decreased narcotic utilization and length of hospitalization [27]. Several medications have been examined for preoperative use in MIS spine surgery. A single 600-1200 mg dose of gabapentin or 100-150 mg dose of pregabalin given one to two hours preoperatively led to a reduction in postoperative pain, anxiety and narcotic consumption during the first 24 postoperative hours and longer time to breakthrough pain analgesia [25,28-31]. Similarly, a 1-2 g preoperative dose of acetaminophen has been shown to reduce postoperative pain and morphine requirements [27] Preemptive multimodal analgesia has also been described. Combining 200 mg of celecoxib, 75 mg of pregabalin, 500 mg of acetaminophen, and 10 mg of extended-release oxycodone one hour prior to surgery, the authors demonstrated reduced postoperative pain scores at all time points compared to patients who only received postoperative IV morphine.

Low and normal dose administration of nonsteroidal anti-inflammatory drugs (NSAIDs) given postoperatively was associated with reduced opiod consumption and pain scores compared to placebo groups; however, high-dose administration of specific NSAIDs (ketorolac, diclofenac, etc.) was associated with reduced fusion rates and should be avoided in fusion procedures. By inhibiting COX, the production of prostaglandins decreased, directly interfering with the pathogenesis of fever, inflammation and pain and is critical in the treatment of various chronic pain syndromes [27]. Jirarattanaphochai and Jung [32] performed a meta-analysis of 10 studies looking at opiate and NSAID use following discectomy or laminectomy. Using a combination of NSAID and opioids resulted in reduced total narcotic consumption and pain scores in comparison to opioids alone. This confirmed the idea that utilizing medications that target differing mechanisms and pathways allow for a synergistic effect, leading to reduced doses of a single medication and its likelihood of adverse side effects. Additional medications used intraoperatively are theorized to have the same effect. Infiltration of the surrounding soft tissue with lidocaine and epinephrine prior to skin incision, as well as the use of 30-40 mLs of ropivacaine 0.5% at skin closure, reduced postoperative pain and opioid consumption [33,34]. Additionally, the use of postoperative epidural analgesia has been associated with significant improvements

in pain scores, reduced postoperative narcotic consumption and nausea, as well as earlier bowel recovery following spine surgery [35,36]. Although varying dosages of medications have been studied, evidence suggests that a combination of medications administered pre-, peri- and postoperatively results in reduced postoperative pain and narcotic consumption with reduced or no significant difference in side effects and provides the basis for multimodal analgesia (MMA) protocols.

The preferred pain management technique is a controversial topic in orthopedic specialties, including spine surgery. Several studies have attempted to determine the most effective practice by comparing PCA and MMA protocols. Many surgeons who utilize MMA protocols combine different medications and dosages depending on their individual experience. The senior surgeon performed a consecutive analysis of 139 patients following minimally invasive transforaminal lumbar interbody fusion (MIS TLIF). Patients were stratified into MMA or PCA cohorts based on the postoperative management they received. The PCA cohort received routine postoperative IV PCA management, while the MMA cohort received preemptive analgesia in the form of Pregabalin (150 mg PO), OxyContin (10 mg PO), Flexeril (10 mg PO), and Acetaminophen (100 mg IV – given in the OR). Intraoperatively the patients received a weight-based dose of Marcaine (0.5% with epinephrine injection prior to incision), Propofol induction, Sevoflurane maintenance, Dexamethasone (10 mg IV), Zofran (4 mg IV), Pepcid (20 mg IV), Fentanyl (<150 mcg IV), and Ketamine (50 mg IV). Postoperatively, patients received Flexeril (10 mg PO), Tramadol (50 mg PO), and Norco (10 mg PO) in the post-anesthesia care unit. On postoperative day 0, patients received Tramadol (50 mg PO Q6H), Norco (10 mg PO Q4H), Flexeril (10 mg PO Q8H), Lyrica (75 mg PO Q12H), Oxycodone IR (5 mg if narcotic naïve; 10 mg if narcotic tolerant PO Q4H PRN pain), and Cryotherapy (ice packs applied to back). Analysis of postoperative outcomes revealed a decrease in postoperative pain, narcotic consumption, and episodes of postoperative nausea/vomiting compared to the PCA cohort, however, this did not translate into a reduced risk of narcotic dependence in the subsequent months following TLIF [37]. Similarly, a prospective study by Garcia, et al. [38] reported decreased total narcotic consumption, lower postoperative pain scores, and time to solid food consumption following lumbar decompression surgery when MMA was used instead of PCA. However, no benefit in complication rates was observed in either cohort. Similarly, retrospective studies by Mathiesen, et al. [6] and Rajpal, et al. [39] demonstrated decreased total narcotic consumption and lower pain scores, as well as fewer adverse side effects such as nausea, vomiting, constipation, drowsiness, coughing and difficulty with deep breathing. An added benefit that has been demonstrated with MMA is shorter time to mobilization and reduced length of hospital stays [6,40] Despite decreased narcotic utilization with MMA protocols, total cost of medication has been reported to be similar between MMA and PCA groups [39]. However, this analysis did not take in to account the up front cost of equipment needed with PCA. Additionally, with an increasing focus on controlling healthcare costs, a rising number of orthopedic spine surgeries are being performed at ambulatory surgical centers with discharge planned for the day of the operation. These shorter hospital stays make the use of intravenous PCA less practical, and alternative pain management strategies are needed [40]. Despite the many advantages seen with MMA, there is no literature describing the optimal MMA protocol or an algorithmic approach to treating patients [41]. However, based on current literature, a successful minimally invasive spine surgery program involves a multidisciplinary team combining several pain management therapies into multimodal analgesia resulting in the successful control of postsurgical pain.

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