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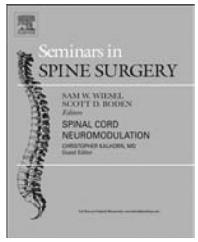

Anesthesia and postoperative pain control following spine surgery

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ABSTRACT

The focus of this manuscript will be to discuss the evidence supporting the various modalities, routes of administration, and timing of analgesic medication in the setting of spine surgery. We outline the evidence supporting multi-modal analgesia and describe strategies to optimize pain control while limiting opioid use. We discuss the importance of pre-emptive analgesia, optimal intraoperative pain regimens and non-opioid alternatives that may be used to help treat post-operative pain. The role of regional anesthesia as an adjunct to oral medications is also discussed.

1. Introduction

Deaths from un-intentional drug overdoses have risen steeply over the past two decades and now represent the second leading cause of accidental death in the United States. The "opioid-epidemic" has been recognized as a grave public health crisis. While the scope of the opioid epidemic demands a multi-faceted approach, post-operative pain management has been identified as an important area of intervention by several authors.[1–3] One recent study estimated that 5.9–6.5% of patients undergoing elective surgery developed new, persistent opioid use.[1] This problem is particularly relevant to spine surgeons as the risk for chronic opioid use is the highest after orthopedic (23.8%) and neurosurgical (18.7%) procedures.[4] Additionally, 99% of patients receive a prescription for at least one opioid pain medication after surgery.[2]

Unfortunately, treatment of post-operative pain with opioid medications is not benign: at least 50% of patients treated with opioid medications experience at least one opioid-related adverse event.[5] In spine surgery, inadequate pain control and increased narcotic use have been associated with increased adverse events, longer length of hospital stays, and higher costs.[5–8]

These findings have led several authors to develop multi-modal analgesic (MMA) strategies that seek to optimize pain control while minimizing opioid use. MMA regimens seek to target the various causes of pain after spine surgery, including: inflammation, muscle spasticity, neuropathic pain, and a lowered central nervous system pain threshold. In addition to targeting multiple sources of pain, MMA regimens attempt to optimize the timing of analgesia. The following sections provide an overview of these strategies.

2. Pre-emptive analgesia

Preemptive analgesia is thought to reduce post-operative pain by prophylactic inhibition of the central autonomic hyperactivity that accompanies painful stimuli. Published protocols include the use of a nonsteroidal anti-inflammatory, acetaminophen, or sustained release opioid from up to two weeks

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to one hour prior to the initiation of surgery.[9,10] Lee et al. analyzed the role of immediate preoperative analgesia with either NSAIDs, Tramadol, COX-2 inhibitors, or opioids across multiple hospital systems in patients undergoing instrumented spinal fusion for degenerative spine disease. They found that pre-emptive analgesia was associated with lower self-reported levels of pain, fewer patients with PCA use, improved activity levels, lower depression scores, and improved self-care when compared to traditional post-operative pain control.[11]

3. Pharmacologic agents

3.1. Nonsteroidal anti-inflammatory drugs (NSAIDs)

Following surgery, prostaglandins play a key role in reducing the pain threshold at both the site of injury and the surrounding uninjured tissues. NSAIDs block prostaglandin production through the inhibition of cyclooxygenase (COX) enzymes, thereby resulting in considerable anti-inflammatory and analgesic effects. COX-2 inhibitors represent a subset of NSAIDs that selectively block the COX-2 isoenzyme while minimizing COX-1 blockade and the associated impact on platelet function and the gastric mucosa. Roberts et al. suggested via Cochrane Review that nonselective NSAIDs and COX-2 inhibitors are both effective in providing analgesia following orthopaedic surgery in the extended postoperative period, with COX-2 inhibitors in particular resulting in minimal side effects.[12]

Despite this potential, spine surgeons have historically approached NSAIDs with caution due to concern for potential postoperative bleeding and bony nonunion. Animal models have suggested that NSAIDs may be involved in the inhibition of osteoblast production and differentiation, and therefore bony metabolism.[13,14] In regards to clinical studies, Glassman et al. found that nonunion rates were higher for patients undergoing lumbar fusion who received a minimum of 60 mg of intramuscular ketorolac compared those who received opioids alone.[15] On the other hand, Pradhan et al. found no difference in nonunion rates between patients undergoing instrumented fusion who received 30 mg of ketorolac every six hours for 48 h and those who did not.[16] More recent evidence suggests that the adverse effects associated with NSAIDs are likely to be dose and/or duration dependent. Li et al., for example, found that short exposure to normal dose NSAIDs was safe after spinal fusion, whereas short exposure to *high* dose ketorolac increased risk of nonunion.[17] Similarly, Dodwell et al. found in a meta-analysis of high quality studies no association between NSAID use and nonunion.[18] In light of this increased use of NSAIDs, Jirarattanaphochai et al. completed a meta-analysis of 17 randomized controlled trials comprising 400 lumbar spine surgery patients who received NSAIDs plus opioid analgesics postoperatively and 389 patients who received only opioids. They found that patients who received NSAIDs and opioids in combination reported lower overall pain scores and less opioid use when compared to patients receiving opioids alone.[19] In a separate study, Jirarattanaphochai et al. randomized patients undergoing lumbar diskectomy, laminectomy, or fusion to receive either parecoxib 40 mg with additional 40 mg doses every 12 h for 48 h postoperatively, or a saline placebo. They found that patients who received parecoxib had a 39% reduction in morphine use, less pain at rest, and greater satisfaction compared to those who did not.[20]

Despite these more recent findings, more work is required to elucidate the relationship between NSAID dose, duration, and the likelihood for adverse outcomes.

3.2. Acetaminophen

Unlike NSAIDs, which inhibit COX enzymes in both the periphery and central nervous system, acetaminophen reduces COX activity primarily in the central nervous system. This allows acetaminophen to function as a powerful analgesic, but with a lesser anti-inflammatory effect.

Acetaminophen has been widely adopted in orthopedic surgery for post-operative pain management. Multiple clinical trials have supported the use of acetaminophen for various types of orthopaedic surgery, including total joint arthroplasty[21] and lower extremity surgery.[22]

Data in spine surgery, however, is more limited. Cakan et al. randomized patients undergoing lumbar laminectomy and diskectomy to receive either 1000 mg of IV paracetamol or a placebo within the concluding 15 min of the operation. They found that intravenous paracetamol did not decrease overall narcotic requirements but was associated with improved postoperative pain scores.[23] Shimia et al. also found that the administration of 1000 mg of IV paracetamol at the conclusion of lumbar diskectomy was associated with improved analgesia and a non-significant decrease in the amount of opioid usage when compared to placebo.[24] Hiller et al. randomized pediatric and adolescent patients undergoing surgery for idiopathic scoliosis to receive either 30 mg/kg IV acetaminophen followed by two additional 30 mg/kg doses every 8 h, or a placebo. They similarly found that there was no difference in opioid consumption between the two groups, but that the acetaminophen group experienced improved postoperative pain scores.[25] Acetaminophen may be an effective and cheaper alternative to other available analgesics, with over half of all patients experiencing adequate postoperative pain control due to acetaminophen alone across a number of subspecialties.[26]

3.3. Anticonvulsant agents

Anticonvulsant drugs such as gabapentin and pregabalin are commonly used in spine surgery patients to treat neuropathic pain. These medications bind the alpha-2 subunit of calcium-gated ion channels and decrease sensory neuron excitability by inhibiting the release of neurotransmitters. These agents may be effective for postoperative analgesia, treatment of spastic pain, preoperative anxiolysis, and prevention of chronic pain.[27] Three independent randomized controlled trials have provided strong support for the continued perioperative use of these agents. Kim et al. randomized patients undergoing instrumented lumbar fusion to receive either 75 mg of pregabalin, 150 mg of pregabalin, or placebo both one hour before surgery and at 12 h following surgery. They found that patients who received 150 mg of pregabalin used