Perioperative Pain Management for Elective Spine Surgery: Opioid Use and Multimodal Strategies

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Key words
- Analgesics
- Elective surgical procedures
- Opioid
- Pain
- Pain management/trends
- Pain syndrome
- Postoperative

Abbreviations and Acronyms
COX: Cyclooxygenase
GI: Gastrointestinal
IV: Intravenous
NMDA: *N*-methyl-D-aspartate
NSAID: Nonsteroidal antiinflammatory drug
RCT: Randomized controlled trial

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Citation: World Neurosurg. (2022) 162:118-125. https://doi.org/10.1016/j.wneu.2022.03.084

Journal homepage: www.journals.elsevier.com/world-neurosurgery

Available online: www.sciencedirect.com

In recent years, physicians and institutions have come to recognize the increasing opioid epidemic in the United States, thus prompting a dramatic shift in opioid prescribing patterns. The lack of well-studied alternative treatment regimens has led to a substantial burden of opioid addiction in the United States. These forces have led to a huge economic burden on the country. The spine surgery population is particularly high risk for uncontrolled perioperative pain, because most patients experience chronic pain preoperatively and many patients continue to experience pain postoperatively. Overall, there is a large incentive to better understand comprehensive multimodal pain management regimens, particularly in the spine surgery patient population. The goal of this review is to explore trends in pain symptoms in spine surgery patients, overview the best practices in pain medications and management, and provide a concise multimodal and behavioral treatment algorithm for pain management, which has since been adopted by a high-volume tertiary academic medical center.

INTRODUCTION

Addiction to opioid drugs claimed more than 33,000 lives in the United States in 2015 (>4 times more than 1999) and more than half involved prescription drugs.[1] This situation is part of a 15-year-long trend that the Centers for Disease Control and Prevention say is a "national epidemic."[2] In addition, estimates of health care costs from prescription opioid abuse reach $25 billion, with excess medical and drug costs accounting for the largest proportion.[3] Researchers have identified numerous contributing factors related to the opioid crisis, including the changing dynamics of the doctor–patient relationship, the creation of more potent and long-acting drugs, and trends started by influential medical experts and academic societies in the late 1990s suggesting that total pain control should be treated as an attainable medical ideal: the so-called fifth vital sign.

For surgeons, the challenge has always existed to effectively manage postoperative pain, because mismanagement can lead to worsened patient-perceived outcomes, worsened quality of life, and increased length of stay in hospital.[4,5] This weighty task is subject to even more external pressures because pain control is part of several metrics included in the Hospital Consumer Assessment of Healthcare Providers and Systems, which in turn is linked to Medicare and hospital reimbursements.[6]

As providers, our goals for postsurgical pain management protocols should include aggressively controlling pain in the immediate perioperative period via a multimodal approach that prevents opioid overuse. There should be consistent education among health care providers and patients about opioids, their risks, appropriate timelines for these medications, and responsible stewardship about opioid use. The purpose of this review is 3-fold: 1) to characterize acute and chronic pain within spine patients; 2) to provide an overview of opioid medications and data pertaining their use; and 3) provide a simple, widely adaptable multimodal medical and behavior treatment algorithm for pain management.

INCIDENCE OF PERSISTENT POSTOPERATIVE PAIN IN SPINE PATIENTS

Pain is often a presenting symptom and indication for spinal surgery. Up to 55% of spine surgery patients have chronic pain preoperatively.[7,8] It is expected that patients experience pain in the acute postoperative setting. However, chronic pain after spine surgery is a known and distinct entity and is sometimes refractory to all interventions. This is a particularly challenging patient population and has a prevalence of 3%–40% depending on the intervention and previous pain history.[9-13]

This population is extremely heterogeneous and multiple factors play a critical role in their management, such as cause of back pain, spinal disease, invasiveness of surgery, and location of surgery. A systematic literature review[12] with aggregate data of 21,180 patients who underwent

single-level discectomy (without instrumentation) showed that patients experienced persistent pain rates in both short-term (6–24 months) and long-term (>24 months) of 3%–34% and 5%–36%, respectively. Wang et al.[13] found that persistent low back pain was seen in 7.2% of patients after posterior decompression and instrumented fusion. Risk factors included preoperative low back pain, surgery segment L5-S1, and preoperative paraspinal muscle degeneration. Postoperative pain is a large and varied problem within the spine surgery population, and it is important that pain control techniques be optimized for these patients.

OPIOIDS

Mechanism of Action

Opioids work by stimulating μ and κ G-protein coupled receptors that are found in both the central and peripheral nervous system. The mechanism of opioid-induced analgesia is believed to be caused by stimulation of descending inhibitory pathways in the midbrain, periaqueductal gray, and nucleus reticularis paragigantocellularis.[14] Importantly, the peripheral effects of opioids lead to side effects such as sedation, respiratory depression, constipation, pruritus, vasodilation, nausea, and vomiting.[15] In addition, because of the G-protein coupled receptor mechanism, chronic opioid use leads to receptor upregulation and tolerance to the drug.[16] Subsequently, patients are at risk for withdrawal effects such as sweating, restlessness, nausea, vomiting, diarrhea, and tachycardia after opioid withdrawal.[16] There is evidence that suggests that opioid tolerance and opioid-induced hyperalgesia may develop in as little as 4 weeks of therapy.[17] Many studies agree that patients who do not experience a clinically meaningful pain relief within 1 month of treatment are unlikely to experience pain relief with longer-term use.[18]

Providers should also consider comorbidities when prescribing opioids. Populations at greater risk for harm are those with sleep apnea, patients with renal or hepatic insufficiency, older adults, and pregnant women.[18] Because stimulation of opioid pathways also leads to euphoria, the other major concern with opioids is the potential for dependence and addiction, which in turn can lead to aberrant drug-seeking behavior, use of other illegal drugs, or medication diversion.[19,20]

Opioids in the Postoperative Setting and Persistent Use

A 2017 population-based study of 36,177 surgical patients[21] showed new and persistent opioid use in 5.9% of patients undergoing minor surgical procedures and 6.5% of patients who underwent major surgical procedures. The relatively small difference between opioid use between major and minor surgeries suggests that prescribing practices, rather than severity of pain, are a major factor.

Another study[22] that evaluated opioid-naive patients after low-risk ambulatory surgery found that use of opioids within 7 days of surgery was associated with a 44% increased risk for use at 1 year. Further, Webster et al.[23] performed a retrospective cohort study of worker's compensation claims, with a sample of 8443 patients reporting new-onset disabling low back pain. These investigators found that those who received early opioid prescriptions at higher morphine equivalents were 6 times more likely to receive late opioid prescriptions (30–730 days later) even after controlling for severity of injury.

Guidelines and Legislations

In 2016, the Centers for Disease Control and Prevention released guidelines for prescribing opioids and recommended that when opioids are used for acute pain, clinicians should use the lowest possible dose of immediate-release medications, and prescribe no longer than 3–7 days.[18] For the summary of other general guidelines, see the **Supplementary Appendix**.[1]

OTHER MEDICATIONS FOR MULTIMODAL ANALGESIA

Acetaminophen

Acetaminophen is a common over-the-counter analgesic agent with dual antipyretic properties that is an effective opioid alternative for moderate pain.[15] The mechanism of action is not fully understood, but it is believed that its analgesic properties are derived from central cyclooxygenase (COX) pathway inhibition, endocannabinoid effect, and modulatory effect on descending serotonergic inhibitory pathways. Although generally well tolerated, acetaminophen can be associated with hepatotoxicity when taken over long periods or given in excess in acute settings.[4] The maximal dose is 4 g/day.[24] It has been shown in numerous studies and meta-analyses with pooled data that when used aggressively in perioperative patients, acetaminophen administration can reduce postoperative pain, the total amount of opioid consumption, and the incidence of vomiting.[4,25] In addition, intravenous (IV) acetaminophen is increasingly being used in perioperative multimodal analgesia, and several teams have shown the benefit of including IV acetaminophen in postoperative spine care.[26,27] Acetaminophen is considered a mainstay treatment for pain and should be optimized in the perioperative setting before escalating management.

Nonsteroidal Antiinflammatory Drugs

Nonsteroidal antiinflammatory drugs (NSAIDs) inhibit the COX-1 and COX-2 enzyme, which are responsible for the conversion of arachidonic acid to prostaglandins. This inhibition of prostaglandins reduces pain and inflammation. COX-1 is active throughout the body and provides routine physiologic functions such as protection of gastric mucosa and vascular hemostasis. COX-2 is expressed mainly by polymorphonuclear leukocytes and macrophages becoming active in response to inflammatory stimuli.[4,15,28,29] These medications are used often in the perioperative setting, but providers should be aware of adverse effects as follows.

Renal failure is a theoretic side effect of NSAIDs, because blood flow to the kidneys is mediated by prostaglandins. In a Cochrane review from 2007, Lee et al.[30] concluded that NSAIDs cause a clinically unimportant and transient reduction in renal function (in those with normal preoperative renal function) and should therefore not be withheld at time of surgery. However, there is a risk in those with preexisting renal insufficiency and NSAIDs should not be administered to

these patients. Gastrointestinal (GI) toxicity may occur and is more common in patients with a history of GI ulcer, older patients, and those with concurrent use of glucocorticoids or anticoagulants.[31]

In addition, NSAIDs, both selective and nonselective, have been implicated in an uptick in cardiac events.[25,32] Balley et al.[33] concluded from a multinational meta-analysis that NSAIDs show a slight risk for myocardial infarction in the first week of use. This effect was mostly seen with high doses and there was no further obvious harm beyond 30 days. However, among healthy adults, many studies found little to no harm with these medications.

For surgeons, the feared complications of NSAIDs are platelet dysfunction and postoperative bleeding.[4,15,28,29] However, a recent meta-analysis[34] pooled the results of 4 prospective studies that evaluated the effect of ibuprofen versus acetaminophen, tylenol 3, or ketorolac controls found no significant difference in postoperative hematoma. A similar meta-analysis of 27 pooled studies[35] found that ketorolac had superior functional pain scores and no increase in of postoperative hematoma compared with opioids or acetaminophens controls.

NSAID use in spinal fusion surgeries is controversial.[29] Intuitively, prostaglandins play a role in modulation of bone formation and healing, and inhibition of its synthesis might impair these processes. In vitro and animal studies are mixed, but several have reported a link to NSAIDs and decreased bone healing and pseudarthrosis. Historically, this link has been difficult to prove in clinical studies given the large amount of heterogeneity in administration of these medications as well as evaluation of nonunion. In a large systematic review regarding perioperative NSAID use during spinal fusion, Sivaganesan et al.[29] concluded that there is no level 1 evidence from human studies linking NSAID use and reduced fusion rates, and nearly all studies reported after 2005 suggest that short-term (<2 weeks) use of NSAIDs is safe for fusion.

Selective COX-2 Inhibitors

COX-2 inhibitors such as celecoxib and rofecoxib are an attractive alternative for pain management because they provide an antiinflammatory effect without the increased risk of bleeding or GI side effects. In a meta-analysis of trials involving preoperative COX-2 inhibitor administration before surgery, there was no difference in intraoperative blood loss between controls and experimental groups but those receiving COX-2 inhibitors showed decreased pain scores, greater patient satisfaction, lower incidence of postoperative nausea and vomiting, and a decrease in analgesic consumption. In addition, this alternative did not increase the incidence of bleeding complications.[36]

PRECISION (Prospective Randomized Evaluation of Celecoxib Integrated Safety vs. Ibuprofen or Naproxen)[37] showed that celecoxib was noninferior to ibuprofen or naproxen regarding cardiovascular safety in intention to treat analysis. In addition, the celecoxib group had significantly fewer GI events. Similar findings were echoed in SCOT (Standard care vs. Celecoxib Outcome Trial) conducted in Europe,[38] except this study included healthy patients without preexisting cardiovascular risk. This study also found an increase in GI complications and bleeding events in the nonselective NSAID group.

In a prospective double-blinded randomized controlled trial (RCT), Sitibumrunwong et al.[39] showed that a single preemptive dose of ketorolac or parecoxib given immediately before spine surgery significantly decreased post—anesthesia care unit pain scores compared with placebo in patients who underwent lumbar spinal fusion. Similarly, Jirattanaphochai et al.[40] showed that when given postoperatively after posterior lumbar discectomy, spinal decompression, or spinal fusion, parecoxib was found to be superior to morphine alone. Adverse events in both placebo and control groups were equivalent.

Gabapentin/Pregabalin

The analgesic effects of gabapentin are also not fully understood, but it is structurally related to the neurotransmitter γ aminobutyric acid. Binding sites within the central nervous system are associated with calcium channels and the α_2-δ_1 subunit and it is believed that these modulate excitatory neurotransmitters.[41] The American Pain Society recommends that clinicians consider use of gabapentin or pregabalin as a component for multimodal analgesia. Both of these components have been shown to reduce opioid consumption and improve postoperative pain scores. In subsequent studies, these components seemed to be most effective when given preoperatively (typical doses evaluated trials with doses of 600 or 1200 mg gabapentin or 150—300 mg pregabalin) and then continued postoperatively.[25]

In 2 large meta-analyses[42,43] that separately evaluated RCTs for perioperative pregabalin and gabapentin versus placebo in lumbar spine surgery, these medications were significantly associated with reduced postoperative pain scores, reduced opioid consumption, and reduced postoperative nausea, vomiting, and pruritus. The gabapentin study also showed a dose-dependent relationship, with higher doses (>900 mg/day) associated with reduced visual analog scale scores, total morphine consumption, vomiting, and urinary retention compared with lower doses (<900 mg/day).

Lidocaine

Lidocaine is an amide anesthetic that is increasingly being used for acute management of postoperative pain. When used for local injection, the primary mechanism of action of lidocaine is through the blockage of sodium channels.[44] Although systemic effects of lidocaine are probably at least partially related to this mechanism, the exact mechanism of IV lidocaine is still being explored.[45] In addition to sodium channel blockade, lidocaine has been shown to block N-methyl-D-aspartate (NMDA) receptors and decrease the concentration of circulating inflammatory cytokines.[44,46] Lidocaine has analgesic, antihyperalgesic, and ant-inflammatory properties.[44] The use of IV lidocaine is also associated with relatively few side effects, including neurologic changes such as lightheadedness, dizziness, and visual disturbances, and cardiac dysrhythmias.[47]

Because of the proven beneficial properties for controlling pain and inflammation, combined with its exceedingly rare side effects, IV lidocaine has become an attractive alternative to opioids for perioperative pain control. Of the studies that have examined the effect of perioperative

Table 1. Comparative Studies with Evidence for the Use of Bupivacaine in Spine Surgery Postoperative Pain Control

Reference	Study Design	Study Arm	Control Arm	Bupivacaine Dosage	Outcome Difference
Chughtai et al., 2020[60]	Retrospective comparative cohort in pediatric patients with spinal deformity	LB + standard perioperative analgesia	Standard perioperative analgesia (10 μg/mL hydromorphone epidural set at 1–2 μg/kg/hour for 48 hours +0.5 mg/kg ketorolac IV every 6 hours +15 mg/kg acetaminophen by mouth every 6 hours + 5–10 mg oxycodone by mouth every 4 hours when required)	20 mL vial diluted 1:1 with normal saline	LB patients showed lower POD 1 pain scores (median VAS score 2 vs. 5), lower opioid consumption (78.2 vs. 129 MME), shorter length of stay (3 vs. 4 days)
Jirarattanaphochai et al., 2007[58]	Randomized double-blinded placebo-controlled trial for posterior lumbar spine surgery	Peridural methylprednisolone + LB infiltrated into the wound	Placebo (normal saline)	80 mg methylprednisolone locally applied to nerve root +30 mL of 0.375% bupivacaine into paravertebral muscles and subcutaneous tissue around the wound	LB patients had lower cumulative postoperative morphine dose (mean difference of 8.24 mg) and postoperative pain (mean difference of 4.58)
Tomov et al. 2018[59]	Retrospective case-control study after TLF	Infiltration of LB subcutaneously during wound closure	No control/otherwise standard perioperative analgesia	40 mL of 1:1 LB and 0.5% bupivacaine without epinephrine infiltrated into paraspinal wound	LB patients had lower IV narcotic use 72 hours postoperatively (5.2 MME vs. 23.7 MME), fewer acute pain service consults (62.5% vs. 78.6%), and less time on PCA pump (31 vs. 47 hours)
Brown et al., 2018[63]	Prospective randomized controlled trial for posterior lumbar decompression and fusion surgery	LB infiltrated into the paraspinal muscles during wound closure	Normal saline control	266 mg LB in a 60 mL suspension	There was no significant difference in 72 hours postoperative opioid requirements (11.6 vs. 13.4 MME) or in VAS pain score (5.8 vs. 4.4) or length of stay (3.6 vs. 3.7 days)
Cloyd et al., 2018[62]	Retrospective matched cohort study of pediatric patients undergoing posterior spinal fusions	Intraoperative LB	No control/standard perioperative analgesia	Unspecified	No significant difference in 72 hours postoperative MME requirement (2.02 vs. 1.76 mg/kg) or pain score AUC during the first 72 hours (109.5 vs. 109.5)
Puffer et al., 2016[61]	Mixed prospective/retrospective observational cohort analysis for patients undergoing lumbar microdiscectomy	LB infiltration into the wound	No control/standard postoperative analgesia	40 mL of 1:1 LB and 0.5% bupivacaine	LB patients spent significantly less time using IV narcotics postoperatively (13.0 vs. 23.3 hours). No significant difference in VAS score in the postoperative period, total MME, or 30-day emergency department visits

LB, liposomal bupivacaine; IV, intravenous; POD, postoperative day; VAS, visual analog scale; MME, morphine milligram equivalents; PCA, patient-controlled analgesia; AUC, area under the curve.

lidocaine use specific to spine surgery, results are varied. Two of the largest studies have shown an association between IV lidocaine and lower pain scores, lower morphine and fentanyl use, fewer 30-day complications, and increased patient satisfaction.[48,49] Contrarily, in a double-blind randomized placebo-controlled trial in patients undergoing posterior arthrodesis, intraoperative lidocaine (1.5 mg/kg bolus followed by 1.5 mg/kg/hour infusion) did not decrease postoperative morphine requirements, pain scores, postoperative nausea, postoperative inflammation, recovery from ileus, length of hospital stay, or quality of life.[50] Furthermore, a 2017 Cochrane study of the effects of perioperative IV lidocaine infusion across all surgical specialties was unable to confirm whether there was any beneficial effect on pain scores, GI recovery, postoperative nausea, or opioid consumption.[51] The effect of perioperative IV lidocaine is still unclear and future controlled trials are necessary.

Lidocaine patches and plasters can also aid in managing postoperative pain, because they offer the potential to continuously apply analgesic effect directly to skin and largely to limit side effects. In

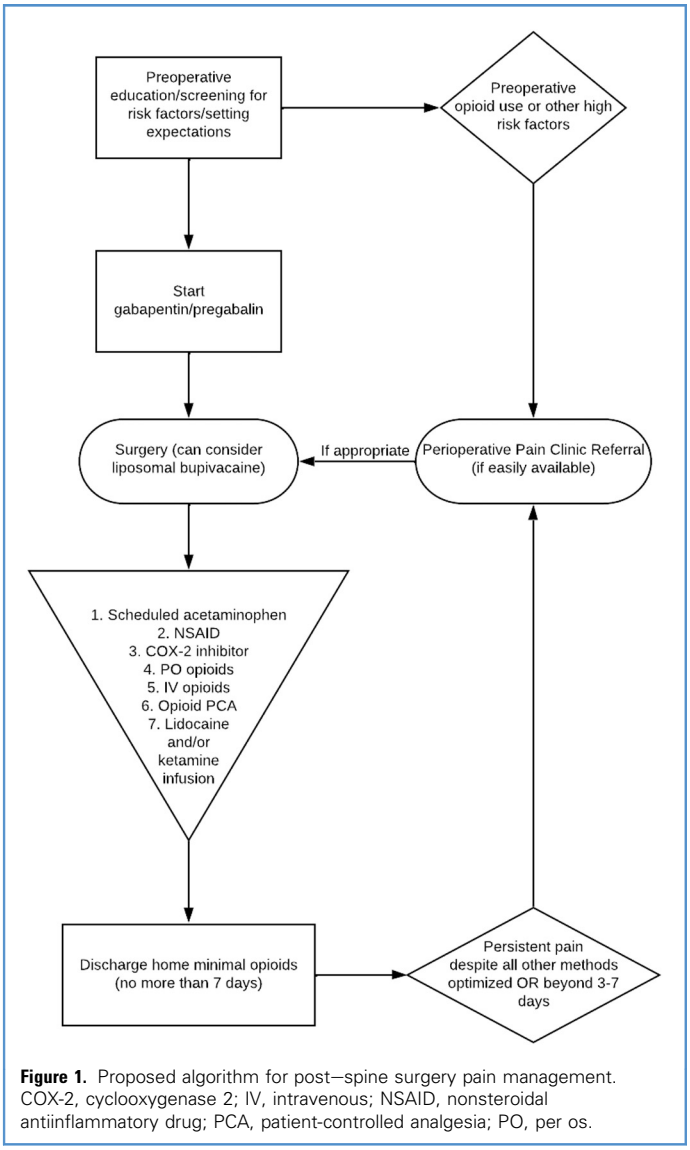

Figure 1. Proposed algorithm for post–spine surgery pain management. COX-2, cyclooxygenase 2; IV, intravenous; NSAID, nonsteroidal antiinflammatory drug; PCA, patient-controlled analgesia; PO, per os.

theory, topical lidocaine may be useful in pain control for perioperative pain control in patients with sensitive wounds. Although most studies have found that topical lidocaine improves pain and pain scores,[52-54] few are specific to spine surgery, and study protocols and end points tend to be heterogeneous, limiting generalizability of findings. Of the few spine surgery studies, Kim[53] found that lidocaine patches provide significant pain control in percutaneous endoscopic lumbar discectomies. Moreover, another study by Takano et al.[54] found that topical lidocaine was associated with significantly lower visual analog scale scores and postoperative diclofenac dose for up to 48 hours in a group of 30 spine surgery patients compared with control patients who received fentanyl infusion. Overall, there are limited data on the efficacy of topical lidocaine for postoperative pain control in spine surgery patients. Future studies are needed to define the pain control benefit and assess the value relative to the added health care costs.

Bupivacaine

Bupivacaine is another amide local anesthetic, similar to lidocaine, which works by inactivating voltage-dependent sodium channels.[55] Overall, the symptomatic profile of bupivacaine toxicity is similar to that of other local amide anesthetics such as lidocaine and includes early neurologic symptoms such as lightheadedness, dizziness, and disorientation, and severe symptoms such as hypotension, arrhythmias, and cardiac and respiratory arrest.[56] Bupivacaine is known to be more potently toxic than other local anesthetics, but complications from local infiltration are more rare.[56] Bupivacaine has become a key facet of multimodal analgesia in perioperative patients, but was originally limited to 8–12 hours of pain relief.[55] Because of this situation, liposomal formulations of bupivacaine capable of providing relief for up to 96 hours have become commercially available.[57] The slower release of liposomal bupivacaine also leads to lower plasma concentrations, and, therefore, fewer adverse effects.[55]

The evidence for the use of bupivacaine in postoperative spinal care is mixed. Generally, studies have found that liposomal bupivacaine injected at the surgical site or nerve root leads to better pain control (whether that be through pain medication use or pain scores).[58-60] However, other studies have failed to replicate this result and there is still debate about the long-term differences in outcomes after the use of local liposomal bupivacaine.[61-63] The relevant studies are summarized in **Table 1**. Overall, there need to be more formal double-blinded RCTs or comprehensive meta-analyses to formally compare these pooled results to arrive at definitive clinical guidelines for the use of liposomal bupivacaine.

Across all studies, there was variability in power, surgery type, multimodal analgesia regimen used outside local anesthetic, and clinical outcomes of interest. It is difficult to say with confidence that the use of local anesthetic does or does not add value to the postoperative pain regimen of spine surgery patients. More robust trials are needed to study meaningful clinical end points, including pain scores, patient satisfaction, length of stay, and cost–benefit comparisons.

KETAMINE INFUSIONS

Ketamine is a phencyclidine derivative that acts as a noncompetitive NMDA receptor antagonist in the brain and

spinal cord and that induces dissociative anesthesia.[64] The NMDA receptor is involved in the amplification of pain signals, the development of central sensitization, and opioid tolerance. Studies have shown that subanesthetic doses of ketamine (≤0.3 mg/kg IV) can induce analgesic properties and can become another part of routine perioperative pain control.[64] However, there is still debate as to the optimal timing (preoperative, intraoperative, and postoperative) and duration of ketamine administration.[65]

A 2018 Cochrane systematic review[66] concluded that the use of perioperative ketamine is an effective way to reduce postoperative analgesic consumption and pain intensity in individuals undergoing thoracic, major orthopedic, or major abdominal surgery. The analgesic properties of ketamine may be more effective in patients with a greater baseline level of pain. In addition, the risk of adverse events caused by the drug were minimal and there was evidence that perioperative IV ketamine also reduces postoperative nausea and vomiting by a small extent. Pendi et al.[65] extended this work by performing another meta-analysis of RCTs, which showed that perioperative ketamine reliably reduces pain scores and opioid consumption within the first 24 hours postoperatively. Although most studies examined the intraoperative use of ketamine, there was no distinction made between intraoperative and postoperative ketamine administration, and dosages also varied by study.

The American Society of Regional Anesthesia and Pain Medicine and the American Society of Anesthesiologists released consensus guidelines on the use of ketamine infusions for acute pain management.[67] The group offered detailed dosing recommendations but broadly recommended that ketamine boluses not exceed 0.35 mg/kg and infusions not exceed 1 mg/kg per hour, but did not offer guidance on timing of administration. In addition, poorly controlled cardiovascular disease, pregnancy, active psychosis, hepatic dysfunction, increased intracranial pressure, and increased intraocular pressure are contraindications to the use of ketamine.

Perioperative ketamine likely improves perioperative pain control and reduces opioid consumption postoperatively. Rigorous future studies should be performed to definitively compare intraoperative versus postoperative ketamine administration, because present comparisons are limited and varied.

Patient Selection and Optimization of Comorbidities

Patients with preoperative pain are more likely to experience severe postoperative pain.[68-71] Identifying these patients early can help in tailoring an appropriate postoperative pain management course. In addition, identifying those with mental health comorbidities, such as major depressive disorder, substance abuse, or antisocial personality disorder, is also prudent because these patients are at higher risk of having postoperative pain issues and higher risk of misuse.[18,19,25] A prospective study of patients with chronic disabling spinal disorders found that there was a significantly higher risk of opioid use disorder in patients with Diagnostic and Statistical Manual of Mental Disorders—IV axis I and II and preinjury substance abuse disorders.[20,72] If possible, detoxification from any substance abuse before surgery likely decreases risk of uncontrolled postoperative pain, drug-seeking behavior, and other complications.

Preoperative Education

Survey results from patients receiving spine surgery show that patients often underestimate the severity of the amount of postoperative pain that there will be and might therefore be unprepared mentally and emotionally.[70] Surgeons should provide patients with realistic expectations about surgery and pain treatments as well as educate them about opioids and their risks.[18]

Postoperative Screening and Referral

In addition to assessing neurologic symptoms in the postoperative outpatient appointments, providers should evaluate pain status and medication needs.[25] As shown earlier, most patients should not be experiencing pain by the time they come to their follow-up appointments. Those who are still struggling with pain and taking opioid medications may be at risk for long-term addiction, and referral to a pain management specialist should be considered.

CONCLUSIONS

Spine surgeries have the potential to be among the most painful surgical procedures that patients can undergo, and opioid addiction continues to be an epidemic with a significant iatrogenic cause. Up to 75% of people entering treatment for heroin addiction report that their first opioids were prescription drugs.[73] Multimodal perioperative analgesia has become the mainstay of effective pain management in these surgical patients. Although there are established recommendations for pain control in surgery broadly, there is varied evidence on the optimal pain control protocols for spine surgery. We have identified spine surgery pain control techniques with the best evidence. Although the details vary slightly based on the type of surgical procedure, general best practices include the use of pregabalin/gabapentin, COX inhibitors, acetaminophen, and judicious opioids. Based on the presented data, we have proposed an algorithm for perioperative pain management in spinal surgery patients (**Figure 1**). There is a growing body of evidence for the use of local anesthetics such as liposomal bupivacaine. It is also likely that perioperative IV lidocaine or ketamine is beneficial. Future studies with rigorous methods and robust power should be conducted to identify the most effective and cost-balanced protocols for perioperative pain control in spine surgery.

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Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Disclosures unrelated to the current work include: K.D.T. is a consultant for Bioventus and receives honoraria from LifeNet Health and DJO; M.M.A.-El-B. is a consultant for Spineology; C.R.G. received grants from the Robert Wood Johnson Harold Amos Medical Faculty Development Program, Burroughs Wellcome Fund, North Carolina Spine Society, and the NIH/NINDSK12NRCDP Physician Scientist Award; C.I.S. is a consultant to Medtronic, Biomet, NuVasive, and Globus, and is a patent holder for Medtronic and Biomet; and I.O.K. is a consultant for NuVasive, receives Fellowship funding from NuVasive, and is a member of the advisory board for Johnson & Johnson Adult Deformity Group. All other authors have no disclosures relevant to the current work, nor any true/perceived conflicts of interest.

Received 17 November 2021; accepted 18 March 2022

Citation: World Neurosurg. (2022) 162:118-125. https://doi.org/10.1016/j.wneu.2022.03.084

Journal homepage: ***www.journals.elsevier.com/world-neurosurgery***

Available online: ***www.sciencedirect.com***

1878-8750/$ - see front matter

SUPPLEMENTARY APPENDIX

CDC RECOMMENDATIONS FOR PRESCRIBING OPIOIDS FOR CHRONIC PAIN OUTSIDE OF ACTIVE CANCER, PALLIATIVE, AND END-OF-LIFE CARE

Determining When to Initiate or Continue Opioids for Chronic Pain

1. Nonpharmacologic therapy and nonopioid pharmacologic therapy are preferred for chronic pain. Clinicians should consider opioid therapy only if expected benefits for both pain and function are anticipated to outweigh risks to the patient. If opioids are used, they should be combined with nonpharmacologic therapy and nonopioid pharmacologic therapy, as appropriate.
2. Before starting opioid therapy for chronic pain. clinicians should establish treatment goals with all patients, including realistic goals for pain and function, and should consider how therapy will be discontinued if benefits do not outweigh risks. Clinicians should continue opioid therapy only if there is clinically meaningful improvement in pain and function that outweighs risks to patient safety.
3. Before starting and periodically during opioid therapy, clinicians should discuss with patients known risks and realistic benefits of opioid therapy and patient and clinician responsibilities for managing therapy.

Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

4. When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids.
5. When opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥50 morphine milligram equivalents (MME)/day. and should avoid increasing dosage to ≥90 MME/day or carefully justify a decision to titrate dosage to ≥90 MME/day.
6. Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.
7. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy. clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids.

Assessing Risk and Addressing Harms of Opioid Use

8. Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk factors for opioid-related harms. Clinicians should incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day). or concurrent benzodiazepine use, are present.
9. Clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or dangerous combinations that put him or her at high risk for overdose. Clinicians should review PDMP data when starting opioid therapy for chronic pain and periodically during opioid therapy for chronic pain, ranging from every prescription to every 3 months.
10. When prescribing opioids for chronic pain, clinicians should use urine drug testing before starting opioid therapy and consider urine drug testing at least annually to assess for prescribed medications as well as other controlled prescription drugs and illicit drugs.
11. Clinicians should avoid prescribing opioid pain medication and benzodiazepines concurrently whenever possible.
12. Clinicians should offer or arrange evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder.

*All recommendations are category A (apply to all patients outside of active cancer treatment, palliative care, and end-of-life care) except recommendation 10 (designated category B, with individual decision making required); see full guideline for evidence ratings.