

Opioid based Anesthesia in Spine Surgery

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Abstract:

Background: Opioid-based anesthesia (OBA) has traditionally played a central role in perioperative analgesia for spine surgery because these procedures are frequently associated with severe nociceptive stimulation and substantial postoperative pain. Opioids provide potent analgesia and sympatholysis through their actions on μ , κ , and δ opioid receptors at spinal and supraspinal levels, thereby suppressing nociceptive transmission and attenuating the surgical stress response. They are commonly used during induction and maintenance of anesthesia and for postoperative pain control because of their rapid onset, reliable efficacy, and ability to reduce anesthetic requirements. However, opioid administration is associated with important dose-dependent adverse effects, including respiratory depression, sedation, nausea and vomiting, gastrointestinal hypomotility, pruritus, urinary retention, tolerance, and dependence. Moreover, patients undergoing spine surgery may require substantial postoperative opioid consumption, particularly those with pre-existing chronic pain or previous opioid exposure, increasing concerns regarding persistent postoperative opioid use and unfavorable surgical outcomes. Therefore, appropriate opioid selection, careful dose titration, and consideration of multimodal analgesic approaches are essential to achieve effective perioperative pain control while minimizing opioid-related complications.

Keywords: Opioid-based anesthesia; Spine surgery; Opioids; Perioperative analgesia; Postoperative pain; Opioid receptors; Multimodal analgesia.

Introduction:

Opioids have traditionally been a mainstay of perioperative analgesia in spine surgery due to the severe postoperative pain associated with extensive tissue dissection and neural manipulation. However, their widespread use has contributed to significant adverse effects and public health concerns. By 2010, opioids were among the most frequently prescribed medications in the United States, and opioid-related mortality has risen markedly since 1999, accounting for the majority of drug overdose deaths (1).

The emphasis on pain as the “fifth vital sign” and adherence to the World Health Organization analgesic ladder have further increased perioperative opioid exposure (2).

Mechanism of Action of Opioids in Anesthesia

Opioid analgesics act primarily through μ , κ , and δ G protein-coupled opioid receptors, which regulate nociceptive transmission at spinal and supraspinal levels (**Table 1**). μ -receptor activation is the main mediator of analgesia and is also responsible for most adverse effects, including respiratory depression, sedation, reduced gastrointestinal motility, tolerance, and dependence (3).

At the cellular level, opioid receptor activation inhibits adenylate cyclase, decreases calcium influx, and increases potassium conductance, resulting in reduced neurotransmitter release and neuronal hyperpolarization, thereby suppressing pain pathways (4).

κ -receptor activation contributes to spinal analgesia and sedation but is commonly associated with dysphoria and psychotomimetic effects, limiting abuse potential. δ -receptors play a minor modulatory role in analgesia and affective pain responses. Differences in receptor affinity and intrinsic activity among opioid classes explain variability in clinical effects and analgesic responses, even at equianalgesic doses (2).

Mixed agonist–antagonist opioids act as partial μ -agonists and may antagonize full μ -agonists, potentially precipitating withdrawal in opioid-dependent patients. Buprenorphine is unique due to its high μ -receptor affinity, slow dissociation, partial agonism, and κ -receptor antagonism, accounting for its prolonged action and resistance to naloxone reversal (2).

Table 1: Opioid receptors and their properties (5).

Receptor	Location	Principal Effects
δ (Delta)	Brain (pontine nuclei, amygdala, olfactory bulb, deep cortex); peripheral sensory neurons	Mild analgesia, antidepressant effects, physical dependence
κ (Kappa)	Brain (hypothalamus, periaqueductal gray); spinal cord (substantia gelatinosa)	Analgesia, sedation, miosis, dysphoria
μ (Mu)	Brain (cortex, thalamus, periaqueductal gray); spinal cord (substantia gelatinosa); peripheral sensory neurons; intestine	Analgesia, respiratory depression, miosis, euphoria, decreased gastrointestinal motility, physical dependence
μ_1	Predominantly peripheral	Central interpretation of pain
μ_2	Central nervous system	Respiratory depression and physical dependence
μ_3	Vascular tissue, leukocytes	Immunomodulatory and vascular effects

Indications for Opioid-Based Anesthesia

Opioid-based anesthesia remains an important anesthetic strategy in selected surgical populations due to the potent analgesic and sympatholytic properties of opioids. OBA is particularly indicated in procedures associated with severe nociceptive stimulation, where opioids provide effective attenuation of the surgical stress response and facilitate hemodynamic stability. Major surgeries such as spine surgery, thoracic procedures, open abdominal operations, and extensive orthopedic interventions commonly rely on opioids as a core component of intraoperative analgesia (6).

OBA is also indicated in patients in whom profound analgesia is required to prevent excessive sympathetic activation, such as those with ischemic heart disease, limited cardiac reserve, or poorly controlled hypertension. By blunting catecholamine release, opioids help reduce myocardial oxygen consumption and perioperative cardiovascular complications in high-risk patients (7).

Intraoperatively, opioids are frequently used to facilitate smooth induction, maintenance, and emergence from anesthesia by suppressing airway reflexes, minimizing movement, and reducing anesthetic requirements for volatile or intravenous hypnotic agents. Postoperatively, opioid-based regimens may be indicated when regional anesthesia techniques are contraindicated, unavailable, or insufficient to control pain (8).

Classification

Opioid analgesics used in anesthesia are traditionally classified according to their chemical structure into phenanthrenes, phenylpiperidines, benzomorphans, and phenylheptamines (3).

Phenanthrenes include morphine (a naturally occurring alkaloid from the opium poppy) and its semisynthetic derivatives such as hydromorphone, codeine, oxycodone, and hydrocodone. Although codeine occurs naturally, its low concentration necessitates commercial synthesis from morphine. Morphine remains the prototypical μ -opioid receptor agonist and serves as the reference standard for opioid analgesia (3).

Phenylpiperidines are synthetic opioids widely used in anesthesia and include fentanyl and its analogs—sufentanil, alfentanil, and remifentanil. These agents were developed through structural modification of meperidine and fentanyl, resulting in potent analgesics with rapid onset and favorable pharmacokinetics for perioperative use (9).

Mixed agonist–antagonist opioids comprise butorphanol, buprenorphine, nalbuphine, and pentazocine. Butorphanol, buprenorphine, and nalbuphine are phenanthrenes, whereas pentazocine belongs to the benzomorphan class. These agents act as weak μ -receptor agonists while exhibiting κ -receptor agonism (except buprenorphine), accounting for their distinctive clinical profile (9).

Routes of Administration and Perioperative Use

Opioids may be administered via oral, intranasal, sublingual, transdermal, rectal, intramuscular, intravenous, and neuraxial routes. In the perioperative setting, intravenous and neuraxial administration are preferred because they provide rapid onset, reliable bioavailability, and precise titration (9).

Intravenous opioids such as morphine, hydromorphone, fentanyl, and sufentanil are central to intraoperative and postoperative analgesia for moderate to severe pain. Morphine requires cautious titration, as sedation often precedes analgesia, increasing the risk of dose stacking. Its active metabolite, morphine-6-glucuronide, accumulates in renal dysfunction and may cause prolonged respiratory depression. Hydromorphone is frequently favored in patients with renal impairment, although its metabolite may produce excitatory neurotoxic effects (9,10).

Patient-controlled analgesia (PCA) allows individualized opioid dosing, improves patient satisfaction, reduces overall opioid consumption, and enhances postoperative respiratory outcomes compared with conventional nurse-administered regimens, provided appropriate patient selection. Continuous basal PCA infusions increase the risk of respiratory depression, particularly in opioid-naïve patients, and are therefore not recommended in this population. Fentanyl and sufentanil are advantageous for PCA due to the absence of active metabolites, with sufentanil offering effective analgesia and a lower incidence of respiratory depression compared with fentanyl (11).

Neuraxial opioids play an important role in perioperative anesthesia and analgesia. Morphine's low lipid solubility allows prolonged spinal and epidural analgesia lasting 12–24 hours, making it suitable for postoperative pain control. In contrast, fentanyl and sufentanil are highly lipophilic, resulting in rapid onset but shorter duration of action; they are commonly combined with local anesthetics or delivered via epidural PCA for sustained analgesia (12).

Use of Agonist–Antagonist Opioids in Anesthesia

Agonist–antagonist opioids are indicated for moderate to severe pain and are typically administered intravenously or intramuscularly. A defining characteristic of this group is the “ceiling effect,” where further dose escalation does not enhance analgesia or respiratory depression beyond a certain threshold. Although once believed to cause less respiratory depression than pure μ -agonists, studies demonstrate dose-dependent respiratory depression similar to morphine until the ceiling effect is reached; however, apnea remains rare even with large doses in healthy patients (9).

Butorphanol has been commonly used in obstetric anesthesia because of its perceived safety profile regarding respiratory depression. Pentazocine is less well tolerated due to higher rates of dysphoria and its sympathomimetic effects, including increased heart rate and circulating catecholamines, which are not observed with butorphanol, nalbuphine, or buprenorphine. Buprenorphine has the highest abuse potential within this group, and formulations combined with naloxone have been developed to reduce misuse (13).

Adverse Effects and Perioperative Considerations

All opioid agonists cause dose-dependent respiratory depression. Morphine administered neuraxially may produce delayed ventilatory depression 6–12 hours after epidural dosing due to cephalad spread within the cerebrospinal fluid. Bradycardia, vasodilation, and hypotension may occur through vagal stimulation and are most commonly associated with fentanyl and its congeners (14).

Fentanyl and related agents may also cause skeletal muscle rigidity, particularly chest-wall rigidity, which can make ventilation difficult or impossible; management includes neuromuscular blockade or opioid antagonism with naloxone. Nausea and vomiting are common perioperative adverse effects, mediated by stimulation of the chemoreceptor trigger zone and vestibular system, especially in ambulatory patients. Rapid bolus administration of morphine can provoke histamine release, leading to hypotension and flushing, whereas fentanyl and sufentanil do not cause histamine release (15).

Additional adverse effects include decreased gastrointestinal motility with constipation and biliary colic, pruritus, miosis, and urinary retention. Pruritus is particularly common following neuraxial opioid administration. Meperidine is associated with the accumulation of its neurotoxic metabolite normeperidine, which can cause tremors, myoclonus, seizures, and delirium. Fatal interactions have been reported in patients receiving monoamine oxidase inhibitors, and the American Pain Society does not recommend meperidine for acute pain management despite its continued use in some settings (9).

Agonist–antagonist opioids generally produce similar adverse effects to pure μ -agonists but with lesser severity. However, they may precipitate acute withdrawal in opioid-dependent patients and must be used cautiously. Importantly, buprenorphine-induced respiratory depression may be incompletely reversible with naloxone, complicating overdose management (9).

Given increased attention to opioid-related adverse effects including persistent postoperative opioid use, opioid misuse, and diversion of surplus opioid prescriptions, there has been a significant shift towards optimizing non-opioid multimodal pain regimens and precision postoperative opioid prescribing. Spine surgery may result in intense postoperative pain and high postoperative opioid consumption, particularly for patients with pre-existing chronic pain or opioid use prior to surgery. In turn, these patients are at greater risk of adverse surgical outcomes including increased length of hospital stay, increased surgical site infections and increased reoperations. Approximately 9% of patients continue to use opioids one year after spine surgery (16, 17).

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