

Review Article

Pain management following spinal surgeries: An appraisal of the available options

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Abstract

Spinal procedures are generally associated with intense pain in the postoperative period, especially for the initial few days. Adequate pain management in this period has been seen to correlate well with improved functional outcome, early ambulation, early discharge, and preventing the development of chronic pain. A diverse array of pharmacological options exists for the effective amelioration of post spinal surgery pain. Each of these drugs possesses inherent advantages and disadvantages which restricts their universal applicability. Therefore, combination therapy or multimodal analgesia for proper control of pain appears as the best approach in this regard. The current manuscript discussed the pathophysiology of postsurgical pain including its nature, the various tools for assessment, and the various pharmacological agents (both conventional and upcoming) available at our disposal to respond to post spinal surgery pain.

Key words: Hyperalgesia, infusion, intravenous, multimodal analgesia, pain management, pain measurement, spinal surgery

INTRODUCTION

Barring few exceptions, spinal surgeries are mostly elective in nature.^[1] Commonly performed spinal surgeries include laminectomies, discectomies, spinal fusions, instrumentations, scoliosis corrections, and spinal tumor excision. Conventional spinal surgeries (nonminimally invasive) often involve extensive dissection of subcutaneous tissues, bones, and ligaments and thus result in a considerable degree of postoperative pain. The pain is severe and typically lasts for 3 days.^[2] Adequate pain relief is, therefore, an important facet of postoperative care of these patients. Adequate pain treatment in these patients is compounded by the

fact that the majority of these patients had already suffered from preexisting chronic pain that had been treated with conventional analgesics or narcotics. The preexisting pain along with long-term consumption of analgesics and/or opioids alters pain perception in these patients thereby complicating pain management.^[3,4] Effective pain controls facilitates early mobilization as well as expedites hospital discharge. This review attempts to discuss the physiological basis of pain following spinal surgeries, assessment of postoperative pain and also analyze the different aspects of the conventional therapies employed for relief from postoperative pain following spinal surgeries.

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PHYSIOLOGICAL GENESIS AND CHARACTERISTICS OF PAIN FOLLOWING SPINAL SURGERIES

Postoperative pain is the result of activation of various pain mechanisms including nociceptive, neuropathic, and inflammatory.^[5] Pain from the back originates from different tissues such as vertebrae, intervertebral discs, ligaments, dura, nerve root sleeves, facet joint capsules, fascia, and muscles. Various nociceptors and mechanoreceptors that are capable of eliciting pain transmit these sensations. Innervation of these structures is via the posterior rami of spinal nerves connected to sympathetic and parasympathetic nerves. Mechanical irritation, compression or postoperative inflammation causes pain. Since extensive cross connectivity of these nerves exists, referred pain is a common occurrence. As compared to postoperative pain, patients with preexisting chronic pain mostly complain of referred pain rather than local or diffuse pain. However, in the postoperative period, pain is more localized and in subjects where referred pain persisted, their visual analog scale (VAS) scores tend to be elevated.^[6] The intensity of postoperative pain is directly proportional to the number of vertebrae involved in the surgery.^[7] Peripheral as well as central sensitization further contributes to the development of increased pain. Moreover, the region of surgery does not seem to have a bearing on the pain severity, and it is similar in surgeries of cervical, thoracic or lumbar spine.^[8,9] Postoperative pain differs from chronic pain in that it is transitory, and gradual improvement occurs in due course of time. This characteristic makes it further amenable to medical therapy as compared to the chronic pain.^[10]

MEASUREMENT OF PAIN FOLLOWING SPINAL SURGERIES

Accurate measurement of postoperative pain is imperative to provide optimum pain relief. Instruments to evaluate pain should be able to measure intensity, quality, its effect on function and quality of life, and the objective assessment of the amount of pain medications. A variety of pain assessment tools can be utilized to quantify the pain in its different dimensions so that appropriate remedial measures can be undertaken. The numerical rating scale and the VAS are well-validated tools to quantify the intensity of pain. More comprehensive and multidimensional inventories like McGill pain questionnaire helps in estimating the neurophysiological and psychological domains of pain.^[11] It allows to identify the location and quality of pain. The Brief Pain Inventory aids in evaluating the effect of pain on general activity, mood, ambulation, relationships, sleep, and work enjoyment. The Roland Morris disability questionnaire and Oswestry disability index (ODI)/neck disability index (NDI) are validated systems that can be utilized in patients with back pain to ascertain their levels of disability due to pain. ODI is favored over Rolland-Morris score because of its feasibility and responsiveness in disabled patients.^[12] NDI is a modification of ODI utilized in patients with cervical

ailments.^[13] For objective assessment of pain medication usage, all narcotic medications can be converted into their respective morphine sulfate equivalents using an equianalgesic dose table where pain relief with 10 mg parenterally administered morphine is used as a reference standard.^[14]

PAIN MANAGEMENT STRATEGIES FOLLOWING SPINAL SURGERIES

Parenteral and oral modalities

Narcotic analgesics

Narcotic analgesics are common and efficacious drugs for the treatment of severe pain and provide excellent pain relief. However, their widespread employment is limited by their unpleasant side effects like respiratory depression, nausea, vomiting, and other opioid-related adverse events. Intramuscular or intravenous delivery of narcotic analgesics provides reasonable degree of analgesia, however, patient-controlled analgesia (PCA) has established superiority in terms of quality of analgesia and ease of use as compared to intermittent divided dosing. Among narcotics, morphine is the first line therapy in the absence of any contraindications or previous adverse effects. Oxycodone affords better control of hallucinations; however, other side effects are similar. Methadone, which is often used as a replacement opioid in therapy for opioid dependency, has been investigated for pain relief following thoracolumbar surgeries. A single perioperative dose reduced the pain scores and narcotic requirement for 72 h following multilevel spinal surgeries.^[15] Being a noncompetitive N-Methyl-D-aspartate (NMDA) receptor antagonist,^[16,17] it mitigates pain and also reduces (or prevents) opioid tolerance.^[18] Its long duration of action decreases the need of PCA. Dosing modifications are needed for patients who have developed tolerance because of their preexisting chronic pain. Their baseline narcotic requirements should be replaced or maintained. The opioid administration should be aimed to be stopped by a particular due date, and opioid requirements should be reassessed during discharge. Patients may require oral narcotic medications following discharge therefore laxatives and antiemetics should be concurrently prescribed.

Nonsteroidal antiinflammatory drugs

These drugs act by blocking cyclooxygenase (COX) enzyme and the subsequent prostaglandin production and inflammatory pathways. They have proven efficacy in ameliorating postoperative pain,^[19] and especially pain following spinal surgeries.^[20-22] Nonsteroidal antiinflammatory drugs (NSAID's) reduce pain, inflammation, fever, and improve postoperative ambulation following spinal surgeries. Exclusive use of NSAID's for providing postoperative analgesia is, however, questionable. Nevertheless, ample support exists that their concomitant administration along with opioids provides better analgesia as compared to either of the two classes of drugs alone.^[23-25] NSAID's can be administered either intravenously (ketorolac, ketoprofen, diclofenac) or orally (ibuprofen, diclofenac, mefenamic acid). Ketorolac provides acceptable degree of

analgesia and also has opioid sparing effects.^[22,24,26] NSAID's are also effective in providing analgesia for pediatric patients undergoing spinal surgeries as adjuvants to opioids providing lower pain scores and fewer opioids related side effects.^[27-29] NSAID's are generally started within 3 days after surgery and continued for 3 or more days. Platelet dysfunction, risk of hemorrhage, gastric ulceration, and renal toxicity are known side effects of these drugs.^[30] Importantly, concerns have been raised regarding the effects of NSAID's on bone metabolism and osteoblastic proliferation.^[30] However, increasing evidence has been gathered over the past few years that impaired bone healing is dependent upon higher doses (120-240 mg/day)^[31] and longer duration^[32] of treatment with ketorolac. COX-2 inhibitors (parecoxib, celecoxib) are a subclass of NSAID's which by their selective action preserves platelet function and gastric mucosa. They are preferred where hemostasis is a cause of concern. However, COX-2 dependent production of PGE2 is essential for adequate skeletal regeneration. This decremental effect in osteogenic potential limits their widespread applicability. Though it had been demonstrated that celecoxib administration 1 h before induction and 12 h thereafter for next 5 days improved pain scores and reduced opioid consumption following spinal fusion surgery without effecting the rates of nonunion.^[33] COX-2 inhibitors are contraindicated in renal dysfunction and should be used cautiously in patients with history of coronary and cerebrovascular diseases.^[30] Additionally, all NSAID's can increase the risk of sodium and water absorption increasing the risk of exacerbating hypertension and heart failure.

Paracetamol

Paracetamol and its prodrug acetaminophen have gained prominence as an efficacious, safe, and cheaper modality to treat postoperative pain when used intravenously. It is helpful in providing analgesia in the immediate postoperative period when gastrointestinal motility is reduced or when rapid analgesia establishment is required. The onset of analgesia begins within 5-10 min of intravenous paracetamol administration. Mechanisms of action of paracetamol are speculative and may involve central and peripheral sites of action,^[34,35] inhibition of prostaglandins,^[36] and inhibition of descending serotonergic pathways.^[37] Paracetamol as the sole agent may not be useful as an analgesic agent^[38,39] nonetheless combination therapy with opioids have shown to result in decreasing opioid consumption substantially.^[40,41] In spite of the popular perception that acetaminophen has opioid sparing effects, some authors have contradicted the claims of reduction in opioid consumption following administration of acetaminophen. Hiller *et al.* demonstrated that even though the use of acetaminophen as an adjuvant provided enhanced pain relief, the consumption of oxycodone did not decrease.^[42] Paracetamol offers a safer option for analgesia in patients where NSAID's need to be avoided in view of bleeding risks, asthma, or renal derangements.

Ketamine

Ketamine is helpful for attenuation of postoperative pain by its direct analgesic effects and preventing the nociceptive

pathway sensitization in the central nervous system. Being a NMDA receptor antagonist, it is believed to reduce or reverse opioid tolerance in patients who are chronic opioid users. The suggested contribution of NMDA receptors in opioid tolerance and development of hyperalgesia supports the effectiveness of subanesthetic doses of ketamine in alleviating postsurgical pain. Studies on patients undergoing spinal surgeries have not yielded any definitive results.^[43] Loftus *et al.* had demonstrated the reduction in postoperative narcotic demand following intraoperative ketamine administration without any side effects.^[44] Subramaniam *et al.* however contradict this view through their investigation that failed to demonstrate any improvement in analgesia following intraoperative and postoperative infusions.^[44] Dysphoria, sedation, diplopia, salivation, nausea, and hallucination restrict the extensive utilization of this drug in pain management practice.

Corticosteroids

Steroid therapy has been postulated to reduce inflammation and reduce scar tissue formation that contributes to postoperative pain. Apart from the anti-inflammatory effects steroids also inhibit expression of phospholipase A2 and supposedly decrease the release of substance P at the dorsal root ganglion.^[45] Investigations conducted by Aminmansour *et al.* had revealed that intravenous administration of 40 mg dexamethasone intraoperatively reduces radicular pain and opioid requirement following surgery for herniated disc.^[46] Similar findings were reported by Watters *et al.* where oral and intravenous steroid administration reduced pain scores, narcotic consumption, and hospital stay.^[47] Intraoperative irrigation with dexamethasone also reduced the duration of hospitalization and narcotic consumption following microdiscectomy.^[48]

Neuraxial techniques

Intrathecal drug administration

Local anesthetics are the commonly used drugs administered via intrathecal route. Other drugs used through this route include opioids and steroids.^[49] Local anesthetics as the sole agent has the drawback of causing motor and sensory block that hinders adequate neurological assessment. Intrathecal morphine and fentanyl can reduce the cumulative opioid demand in patients after spinal surgery.^[50,51] However, intrathecal opioids, especially morphine can cause late respiratory depression owing to its hydrophilicity and cephalad diffusion through cerebrospinal fluid. Thus, vigilant monitoring is necessary. Combining local anesthetics with opioids provides synergistic effects that reduced opioid dosage and side effects.

Epidural drug administration

Epidural drug administration provides good safety, extended analgesia and decreased incidences of respiratory and thromboembolic events making it a promising route of drug delivery for postoperative analgesia. Epidural analgesia produces substantial reduction in pain scores and narcotic consumption. Local anesthetics, narcotics, and steroids are the usual drugs that are used epidurally. Epidural administration of drugs is

through different techniques such as single and double catheters, intermittent boluses, PCA devices, or continuous infusions. Epidural catheters can be placed intraoperatively by surgeons under direct vision which increases the success rates. Local anesthetics used exclusively carries the risk of motor block and sympathectomy mediated hypotension. Compared to bupivacaine, ropivacaine offers better systemic safety margin and higher selectivity toward sensory fibers. Opioids can also be administered solely or in combination with local anesthetic solutions. Opioids modify the nociceptive input at the levels of dorsal horn receptors. Guilfoyle *et al.* found lower VAS scores following epidural use of fentanyl boluses in patients undergoing lumbar decompression.^[52] Use of opioid only solution through epidural route can predispose to side effects such as nausea, vomiting, and pruritus. Combination solution of opioids and local anesthetics avoids these effects, lowers dosage of parenteral opioids,^[53] and provides better quality of analgesia.^[54,55] Moreover, the relief from dynamic pain is enhanced following use of combination solutions. O'Hara *et al.* and Fisher *et al.*^[56,57] showed that both intravenous PCA and epidural PCA are equally effective; however, greater incidences of side effects were seen in the epidural group.^[57] As with intrathecal usage, epidural administration of opioids should be monitored cautiously to prevent inadvertent respiratory depression due to the diffusion of opioids in cerebrospinal fluid. Epidural administration of steroids is also a promising option as steroids reduce immediate and late pain due to peridural fibrosis. They significantly decrease the analgesic consumption and length of hospital stay following lumbar spinal surgeries.^[58] Adverse events like postoperative wound infection have been rare complications with their usage. Cautious use of epidural techniques is advocated in patients on chronic anticoagulant therapy and those receiving anti platelet drugs considering the risk of developing spinal hematoma.

Newer possibilities for postspinal surgery pain management

Alpha 2 adrenoceptor antagonists

Both clonidine and dexmedetomidine have emerged as effective agents for providing analgesia post spinal surgery. Use of these agents as adjuncts to local anesthetics, opioids or their combination enhances the analgesic properties. Hemodynamic stability and lack of respiratory depression are added advantages of these drugs. Clonidine has been utilized for providing postoperative analgesia through various methods. Administered epidurally, along with subcutaneous bupivacaine at the incision site has shown better analgesia and hemodynamic stability in spinal surgery patients.^[59] Double catheter approaches using bupivacaine, fentanyl, and clonidine has shown encouraging results.^[60] It has also been seen to reduce morphine requirements by 43% in the first 36 h following spinal surgeries.^[61]

The higher affinity and selectivity of dexmedetomidine aid in decreasing the dosages as well as adverse effects of local anesthetics and opioids when used simultaneously with dexmedetomidine. As an adjunct to propofol based total intravenous anesthesia, it has been found to reduce postoperative

pain beyond the immediate postoperative period (48 h) and reducing PCA requirements. Dexmedetomidine presumably acts on the nociceptive cascade and prevents the sensitization of nociceptors present in the dorsal horn. Moreover, the opioid-induced hyperalgesia that might occur following intraoperative opioid usage can be negated using a dexmedetomidine based infusion intraoperatively which extends its effect beyond its duration of action.^[62] When used concurrently with inhalation anesthetics in the form of intravenous infusion, dexmedetomidine reduced analgesic needs postoperatively.^[63] Early recovery provided with dexmedetomidine also allowed early neurological assessment that is important following spinal surgeries.

Transcutaneous electrical nerve stimulation

It has been investigated to be an efficient and opioid sparing method for providing analgesia following major spinal surgery. Transcutaneous electrical nerve stimulation (TENS) applied preincisionally and postoperatively reduces the postoperative opioid requirement and provides sufficient analgesia. However, the beneficial effects of TENS on cognitive functions could not be demonstrated.^[64]

Extended release formulations

These drugs have generated interest because of their longer duration of action. Multivesicular liposomes containing bupivacaine produces sustained release of drugs in the vicinity of the surgical site.^[65] Single dose administration at the surgical site produces analgesia for several days. The effectiveness of these liposomes has been seen in various surgeries; however, their application in spinal surgeries has not been studied. Similar to them, extended release epidural morphine has been developed which can be administered at the lumbar level. Longer lasting analgesia (up to 48 h),^[66] lower systemic concentrations of morphine and better patient activity levels^[67] are the advantages offered by this modality which makes it a novel and emerging approach to manage post spinal surgery pain.

THE CHALLENGE FOR THE FUTURE RESEARCH

A recent review of 179 surgical procedures has rated spinal surgeries among the top six procedures causing highest degree of postsurgical pain.^[68] Adequate and energetic pain management is imperative to improve the functional outcome after surgery. As inadequately treated postsurgical pain contributes to longer hospital stays, slower progress in ambulation, respiratory complications, venous thrombosis, development of chronicity functional deficits and finally elevated cost of treatment, the importance of managing postsurgical pain following spinal surgery cannot be underestimated. Despite improvements in pain management therapies and drugs, a single drug or therapy is yet to be labeled as the "gold standard" for pain control following spinal surgery and wide-ranging differences exist in treatment modalities among different centers. Experts strongly suggest the inclusion of multimodal analgesia for the management

of such patients as the quality of analgesia is improved vastly and the side effects of individual drugs diminish. Moreover, the dependence on opioid also reduces markedly. Thus, it appears as the ideal strategy in the present times. Although multimodal analgesia is the recommended strategy for postoperative analgesia, lack of consensus also exists on the appropriate multimodal analgesia protocols or algorithms.^[69] The identification and utilization of such strategies should be the direction of future research.

CONCLUSION

Effective pain control aided by the judicious use of different pain control therapies can significantly improve the overall success of the surgery. Keeping a proper pain control plan following surgery and discussing it with the patient so that realistic expectations are set in place about the type and level of pain can go a long way in improving the comfort and satisfaction of the patients.

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There are no conflicts of interest.

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