The Effect of Multimodal Analgesia on Intraoperative Morphine Requirement in Lumbar Spine Surgeries

Keelara Shivalingaiah Savitha, Radhika Dhanpal, Apoorwa N. Kothari
Department of Anaesthesia, St. John’s Medical College Hospital, Bengaluru, Karnataka, India

Abstract

Background: Lumbar spine surgery demands intense analgesia. Preemptive multimodal analgesia (MMA) is a novel approach to attenuate the stress response to surgical stimulus. Aims: The aim of the study was to assess the intraoperative morphine consumption in patients undergoing lumbar spine surgery. Patients and Methods: A randomized, prospective, double-blind study involving 42 patients belonging to the American Society of Anesthesiologists Class I and II scheduled to undergo elective lumbar spine surgery were allocated into two groups of 21 each. Group A (study group) received injection diclofenac sodium, paracetamol, clonidine, and skin infiltration with bupivacaine adrenaline and Group B (control group) received paracetamol and skin infiltration with saline adrenaline. Preemptive analgesia was practiced in both the groups. Intraoperative morphine consumption was documented. Statistical Methods: Intraoperative morphine consumption between the two groups was compared using Mann–Whitney U-test. Postextubation sedation score between the two groups was compared using Chi-square test and presented as number and percentage. P < 5% was considered statistically significant. Results: Intraoperative morphine consumption was significantly low in the study group (P < 0.001). Postextubation sedation score was comparable between the two groups. Conclusion: Preemptive MMA has demonstrated significant morphine sparing effect intraoperatively in patients undergoing lumbar spine surgeries.

Keywords: Bispectral index, hemodynamic parameters, lumbar spine surgery, morphine, multimodal analgesia, preemptive analgesia

Introduction

Analgesia is an integral part of balanced anesthesia. Pain is one of the primary concerns of surgeons during spine surgeries because it influences the clinical outcome and patient well-being in the postoperative period.[1,2] Studies with single analgesics (opioid) have not been able to provide effective pain relief peripherally without adverse effects.[3-6] Multiple boluses or continuous infusion of opioids peripherally may result in opioid-induced hyperalgesia.[7,8] With the above concerns, studies combining a strong opioid with a nonopioid drug (nonsteroidal anti-inflammatory drugs [NSAIDs], acetaminophen, alpha two agonist, local anesthetics, etc.) have escalated.[2-4,8-14] However, pain is one of the most common causes of delayed discharge.[2]

The concept of multimodal analgesia (MMA) is however not new.[15,16] Studies so far have not shown MMA to improve postoperative outcome significantly.[2,9] It is due to the mismatch of scientific advances not being incorporated into clinical practice in pain management. The term MMA was coined in the early 1990s, but even now, it does not have a standard protocol to be followed.[19] MMA has not been clearly defined even in the “Recent advances in MMA 2012.”[17] MMA is a rational approach to treat acute pain where all four elements of pain processing, (1) transduction, (2) transmission, (3) modulation, and (4) perception are targeted. It can be achieved by individually tailored dosage of nonopioid drugs with different mechanisms of action, along with smaller doses of opioid.[11,12,18] It can be practiced with the drugs available and a novel thought.

The aim of the study was to assess the intraoperative morphine consumption with MMA in patients undergoing lumbar spine surgery as it is one of the most painful surgeries demanding intense analgesia with hypotensive anesthesia.[19]

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Address for correspondence: Dr. Keelara Shivalingaiah Savitha, 1020, 25th Main, 38th Cross, 4th T Block, Jayanagar, Bengaluru - 560 041, Karnataka, India.  
E-mail: drsavitha ks@yahoo.com

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**Patients and Methods**

This randomized, prospective, double-blind clinical study was carried out in a Tertiary Care Center after obtaining the Institutional Review Board approval and informed written consent from the patients. Forty-two patients scheduled for lumbar spine surgery lasting <5 h between 20 and 65 years, of both sex, with body mass index of 18–30 belonging to the American Society of Anesthesiologists physical Status I and II were included in the study. Pregnant women, patients with bronchial asthma, and known drug allergy undergoing spine surgery were excluded from the study. Patients were randomly allocated into two groups (n = 21), Group A (MMA group/study group) and Group B (conventional regime group/control group) by allocation sequence generated by computer-generated random number table.

Confirming the preanesthetic evaluation and consent, mandatory monitoring with bispectral index (BIS) and train of four (TOF, neuromuscular monitor) was instituted for monitoring throughout the surgery. For drug and fluid administration, intravenous access was secured. Patients were oxygenated by O₂ mask during study drug administration. All patients received midazolam 0.03 mg/kg, ondansetron 4 mg, and glycopyrrolate 0.2 mg intravenously. Study drugs were prepared by assigned postgraduate students who were not participating in the study. Analgesic drugs were administered preemptively in both the groups before induction, providing sufficient time for the onset of action. MMA group received diclofenac sodium, paracetamol, and clonidine intravenously and skin infiltration with bupivacaine adrenaline. Conventional regime group received paracetamol intravenously and skin infiltration with saline adrenaline. Following study drug administration, patients were preoxygenated with 5 L 100% O₂ for 3 min. Fentanyl 3 μg/kg was given to all patients 2 min before induction with propofol, followed by atracurium 0.5 mg/kg to facilitate endotracheal intubation. Anesthesia was maintained with isoflurane in 60% N₂O, and O₂, and divided doses of atracurium. End-tidal CO₂ and end-tidal isoflurane concentration were continuously monitored using an infrared gas analyzer. The goal of anesthesia was to maintain the intraoperative heart rate (HR) and systolic blood pressure (SBP) within ±10% of preinduction values and a BIS of 50–55. For the rise in HR and SBP up to 20% from the preinduction value, morphine 2 mg bolus was administered, if the rise was more than 20%, morphine 0.075 mg to 0.1 mg/kg was administered intravenously by the anesthesiologist monitoring the patient. At the conclusion of surgery, all patients were allowed to recover spontaneously to TOF of T₂. Residual neuromuscular blockade was reversed with glycopyrrolate 10 μg/kg and neostigmine 50 μg/kg. Tracheal extubation was done when the following criteria were met: BIS: 85–88 and TOF T₁/T₂ ratio ≥0.9. For statistical analysis, intraoperative morphine consumption and postextubation observer’s assessment of sedation score [Table 1] at 15 min following extubation were considered.

Adverse effects of analgesic drugs, such as intraoperative bradycardia (opioid, clonidine) bronchospasm, gastritis (NSAID’s), postoperative nausea, vomiting, and respiratory depression (opioid) were recorded.

**Statistical methods**

The present study was nested within a study “the effect of multimodal perioperative analgesia on stress response to surgery and on postoperative pain score.” The present study primary objective was to assess the difference in intraoperative morphine consumption between preemptive MMA group and conventional analgesic regime group for BIS of 50–55 and hemodynamic parameters within ±10% of preinduction value in patients undergoing elective lumbar spine surgeries. The median morphine requirement was 7 mg in the control and 2 mg in the study group; we observed a difference of 5 mg in the morphine requirement between study and control group. Power analysis showed that the sample size of 30 in each group would have adequate power of above 90% to observe a minimum difference of 2 mg morphine requirement between the study and the control group. The distribution of all continuous data was examined using Q-Q plots. Intraoperative morphine consumption between the two groups (study and control groups) was presented as median, first, and third quartile and was compared using Mann–Whitney U-test. Postextubation sedation score between the two groups were compared using Chi-square test and presented as number and percentage. P < 5% was considered statistically significant. Data were analyzed using

| Responsiveness                              | Speech       | Facial expression | Eyes                      | Score |
|---------------------------------------------|--------------|-------------------|---------------------------|-------|
| Responds readily to name spoken in normal tone | Normal       | Normal            | Clear, no ptosis          | 5     |
| Lethargic response to name spoken in normal tone | Mild slowing | Mild relaxation   | Glazed or mild ptosis (less than half the eye) | 4     |
| Responds only after name is called loudly and/or repeatedly | Slurring or prominent slowing | Marked relaxation | Glazed and marked ptosis (half the eye or more) | 3     |
| Responds only after mild prodding or shaking | Few recognizable words |                   |                           | 2     |
| Does not respond to mild prodding or shaking |              |                   |                           | 1     |
RESULTS

The demographic data were comparable in both the groups. The intraoperative morphine consumption was significantly higher in the control groups $P < 0.001$ [Table 2] for BIS of 50–55 and HR and SBP within ±10% of preinduction values. Postextubation in the control group, 61.9% of the patients, had sedation score of three compared to 33.3% in the study group. Between the two groups, the sedation score was statistically insignificant [Table 3]. Postextubation, adverse effects were not observed in the study group, but in the control group, majority of the patients had nausea and a few had vomiting.

DISCUSSION

The study hypothesis was that preemptive MMA will significantly reduce intraoperative morphine consumption with least adverse effects.

Preemptive analgesia is not just a relative timing of intervention; it is an effective proactive approach to treat pain before it is initiated to obtain the maximum clinical benefit of analgesics administered.[13,20,21]

MMA is a rational way to treat acute pain.[2,9,11,13,15,16] It captures the effectiveness of individual nonopoid analgesic agents resulting in additive analgesia with morphine sparing effect[2,9] and is rapidly becoming the standard of care throughout the world.[13]

Morphine was the gold standard analgesic used to treat moderate-to-severe pain. It not only alleviates perioperative pain and anxiety but also decreases somatic and autonomic responses to airway manipulation, improves hemodynamic stability, and reduce minimum alveolar concentration of inhaled anesthetics.[22] However, all this comes at the cost of increased postoperative complications.[2,9,10,23] Hence, morphine is increasingly taking the role of “rescue analgesia” in the progress of acute pain management.[13]

In the present study, to balance the analgesic effects of MMA against an increased risk of perioperative hypotension and bradycardia, precaution was taken to match drug effects and duration of action, with that of surgery. Morphine was the rescue analgesic to treat intraoperative stress response[23] because once titrated doses of nonopioid analgesics of MMA were administered, if there was further demand for analgesics, escalating their doses could manifest with toxic effects or it could lead to complications.

Clinical trials in the literature have focused on postoperative morphine consumption, along with nonopioid analgesics. Their results have shown morphine sparing effect, but the incidence of adverse effects such as nausea, vomiting, pruritus, and/or urinary retention was similar or insignificant between the study group and the control group.[3-5,10,14,17] Inference was that reduction in morphine consumption with conventional analgesic regime had not made a revolutionary change.

The study objective was to assess the difference in intraoperative morphine consumption between preemptive MMA group and conventional analgesic regime group for BIS of 50–55 and hemodynamic parameters within ±10% of preinduction value in patients undergoing elective lumbar spine surgeries.

Depth of balanced anesthesia was monitored by hemodynamic parameters, BIS monitoring, and TOF monitoring to alleviate intraoperative stress response with appropriate interventions. Intraoperative stress response causes not only hemodynamic disturbances but also adds to perioperative morbidity and/or precipitates the preexisting medical conditions, which is a well-known fact.[24,25]

In the study group, morphine consumption was 2 mg compared with 7 mg in the control group, a 3-fold reduction which is statistically significantly $P = 0.001$ [Table 1]. Similarly, other supporting studies on morphine with one or two nonopioid analgesics such as paracetamol, diclofenac sodium, local infiltration of local anesthetic, and alpha two agonists have shown reduction in morphine consumption, demonstrating the analgesic efficacy of those drugs.[3,5,10,17] A “systematic review” in 2010 suggests a combination of paracetamol and NSAIDs may offer superior analgesia compared to administration of either of the drugs.[12] In brief, MMA drugs have additive and/or synergistic effect resulting in intense analgesia[9] with significant morphine sparing effect and is justifiable.

Postextubation 61.9% in the control group had sedation score of three compared to 33% in the study group which was clinically significant, but between the two groups, it was not statistically significant $P = 0.716$ [Table 3]. This infers that
there is some amount of sedation with nonopioid analgesics. The results of the present study were equivocal with morphine sparing studies, where difference in sedation score between the two groups was insignificant.\[^{[1,4]}\]

None of the patients in MMA group had nausea and/or vomiting. In the conventional regime group, the majority of the patients had nausea and few had vomiting. In several morphine sparing studies, both control and the study group had nausea and/or vomiting.\[^{[3,5,10]}\] Results of the study show that nonopioid analgesics are effective in reducing the incidence and the intensity of adverse effects of morphine. Further studies are needed to validate the beneficial effects of the study results.

**Conclusion**

Practicing MMA is justifiable provided patient factors, surgical demand and the available non-opioid drugs are judiciously administered. Preemptive MMA has demonstrated significant morphine sparing effect intraoperatively with least adverse effects in patients undergoing lumbar spine surgeries. The goal of anesthesiologists and surgeons worldwide is to provide "pain-free" recovery to all the patients who undergo surgical procedure. Preemptive MMA can be recommended as one of the modality to attain this goal.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Urban MK. Anaesthesia for orthopaedic surgery. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015. p. 2386-406.
2. Vadivelu N, Mitra S, Narayan D. Recent advances in postoperative pain management. Yale J Biol Med 2010;83:11-25.
3. Delbos A, Bocard E. The morphine-sparing effect of propacetamol in orthopedic postoperative pain. J Pain Symptom Manage 1995;10:279-86.
4. Rokemann MG, Seeling W, Bischof C, Borstinghaus D, Steffen P, Georgieff M. Profilactic use of epidural mevipacaine/morphine, systemic diclofenac, and metamizole reduces postoperative morphine consumption after major abdominal surgery. Anaesthesia 1996;84:1027-34.
5. Alimian M, Pourmajaflian A, Kholdebarin A, Ghodraty M, Rokhtaban F, Yazdkhasti P. Analgesic effects of paracetamol and morphine after elective laparotomy surgeries. Anesth Pain Med 2014;4:e12912.
6. Bashandy GM, Elkholy AH. Reducing postoperative opioid consumption by adding an ultrasound-guided rectus sheath block to multimodal analgesia for abdominal cancer surgery with midline incision. Anesth Pain Med 2014;4:e18263.
7. Silverman SM. Opioid induced hyperalgesia: Clinical implications for the pain practitioner. Pain Physician 2009;12:679-84.
8. Lee M, Silverman SM, Hansen H, Patel VB, Manchikanti L. A comprehensive review of opioid-induced hyperalgesia. Pain Physician 2011;14:145-61.
9. Jin F, Chung F. Multimodal analgesia for postoperative pain control. J Clin Anesth 2001;13:524-39.
10. Hernández-Palazón J, Tortosa JA, Martínez-Lage JF, Pérez-Flores D. Intravenous administration of propacetamol reduces morphine consumption after spinal fusion surgery. Anesth Analg 2001;92:1473-6.
11. White PF. The changing role of non-opioid analgesic techniques in the management of postoperative pain. Anesth Analg 2005;101 Suppl:55-22.
12. Ong CK, Seymour RA, Lirk P, Merry AF. Combining paracetamol (acetaminophen) with nonsteroidal antiinflammatory drugs: A qualitative systematic review of analgesic efficacy for acute postoperative pain. Anesth Analg 2010;110:1170-9.
13. Elvir-Lazo OL, White PF. The role of multimodal analgesia in pain management after ambulatory surgery. Curr Opin Anesthesiol 2010;23:697-703.
14. Blandusz G, Lysakowski C, Elia N, Tramèr MR. Effect of perioperative systemic α2 agonists on postoperative morphine consumption and pain intensity: Systematic review and meta-analysis of randomized controlled trials. Anesthesiology 2012;116:1312-22.
15. Bhuvanendran A. Multimodal analgesia for perioperative pain management. International Anaesthesia Research Society 2011; Review Course Lectures: 58-62.
16. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth 1997;78:606-17.
17. Young A, Bhuvanendran A. Recent advances in multimodal analgesia. Anesth Analg Clin 2012;30:91-100.
18. Macres SM, Moore PG, Fishman SM. Acute pain management. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, editors. Clinical Anesthesia. 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2009. p. 1473-504.
19. Horlocker TT, Wedel DJ. Anaesthesia for orthopaedic surgery. In: Barash PG, Cullen BF, Stoelting RK, Cahalan MK, Stock MC, editors. Clinical Anesthesia. 6th ed. Philadelphia: Lippincott Williams and Wilkins; 2009. p. 1473-504.
20. Mishra AK, Afzal M, Mookerjee SS, Bandyopadhyay KH, Paul A. Pre-emptive analgesia: Recent trends and evidences. Indian J Pain 2013;27:114-20.
21. Khan AA, Sofi SA, Bashir F, Rather MA. A comprehensive study showing efficacy of preemptive intravenous paracetamol in reducing postoperative pain and analgesic requirement in laparoscopic cholecystectomy. J Evol Med Dent Sci 2015;4:10771-7.
22. Fukuda K. Opioid analgesics. In: Miller RD, Cohen NH, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Young WL, editors. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015. p. 864-914.
23. Jain AK, Kumar S, Tyagi A. Practice trends in use of morphine for control of intraoperative pain: An audit. J Anaesthesiol Clin Pharmacol 2012;28:62-5.
24. Lowenstein E. Perianesthetic ischemic episodes cause myocardial infarction in human – A hypothesis confirmed. Anesthesiology 1985;62:103-6.
25. Prys-Roberts C, Greene LT, Meloche R, Fóex P. Studies of anaesthesia in relation to hypertension. II. Haemodynamic consequences of induction and endotracheal intubation. Br J Anaesth 1971;43:531-47.