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RESEARCH ARTICLE
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A COMPARATIVE STUDY OF EFFICACY OF INTRAVENOUS LOXICARD VERSUS KETAMINE INFUSION FOR PERIOPERATIVE OPIOID-SPARING ANALGESIA IN PATIENTS UNDERGOING ELECTIVE SPINE SURGERY: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Elective spine surgery causes moderate-to-severe postoperative pain. Opioids remain the mainstay of analgesia but carry risks of respiratory depression, hypotension, sedation, nausea, vomiting and ileus. Non-opioid adjuncts such as intravenous lidocaine (Loxicard) and ketamine are used in opioid-sparing multimodal analgesia.

Objective: To compare intraoperative Loxicard versus ketamine infusion, against saline control, for perioperative opioid consumption and pain severity in elective spine surgery, and to assess haemodynamics, side effects and satisfaction.

Methods: In this prospective, randomized, three-arm study, 93 of 100 assessed patients were randomized 1:1:1 to Loxicard (L, 1.5 mg/kg loading and maintenance), Ketamine (K, 0.2 mg/kg loading and maintenance), or saline control (CG), 31 per group. Heart rate and mean arterial pressure were recorded at baseline and pre-specified intervals. Primary outcome was perioperative rescue opioid consumption; secondary outcomes were haemodynamics, side effects and satisfaction. Continuous variables were analysed by one-way ANOVA, categorical variables by chi-square test (SPSS v21.0); $p<0.05$ was significant.

Results: All 93 randomized patients completed the study. Mean rescue opioid consumption was lowest in Group L (7.50±5.38), intermediate in Group K (10.20±6.30), and highest in Group CG (14.30±7.10) (ANOVA $p<0.0001$). Loxicard differed significantly from ketamine (mean difference −2.7, $p=0.041$) and both drugs differed from saline (both $p<0.0001$). Baseline HR and MAP were comparable across groups

(p=0.727, p=0.136), but HR and MAP were significantly lower in Groups L and K than CG from the earliest recorded time point onward (p<0.05), with Loxicard showing the greatest attenuation.
Conclusion: Both Loxicard and ketamine infusion reduced perioperative opioid consumption and attenuated haemodynamic stress responses versus saline, with Loxicard showing a marginally greater effect. Both are promising opioid-sparing multimodal analgesic adjuncts for spine surgery; data on pain scores, adverse effects, satisfaction and baseline demographics were unavailable in the source material and are required from the authors before the findings can be considered complete.

Keywords: Lidocaine; Ketamine; Analgesia; Spine; Pain, Postoperative; Analgesics, Opioid; Randomized Controlled Trial as Topic (MeSH terms)

Introduction

Elective spine surgery, ranging from single-level discectomy to multilevel instrumented fusion, is associated with substantial tissue trauma and a pronounced local and systemic inflammatory response. The majority of patients undergoing these procedures experience moderate-to-severe pain in the immediate postoperative period, which delays early mobilisation, prolongs hospital stay and adversely affects patient satisfaction and quality of recovery [1,4]. Across surgical disciplines more broadly, postoperative pain remains inadequately controlled in a large proportion of patients, with pooled data suggesting that moderate-to-severe pain affects roughly a third of patients in the first 24-48 hours after major surgery despite the routine use of analgesic medication [4].

Opioids continue to be the cornerstone of perioperative analgesia because of their potent and reliable analgesic effect. However, opioid-based regimens carry a well-recognised burden of dose-related adverse effects, including respiratory depression, hypotension, sedation, nausea, vomiting, urinary retention and postoperative ileus. In the context of spine surgery in particular, excessive opioid use can also mask evolving neurological deficits, delay recognition of surgical complications, and contribute to the development of persistent postsurgical opioid dependence. These concerns have driven a shift toward multimodal, opioid-sparing analgesic strategies as part of Enhanced Recovery After Surgery (ERAS) pathways, which combine non-opioid agents acting through complementary mechanisms to reduce total opioid exposure while maintaining effective analgesia [10]. The ERAS Society consensus statement for lumbar spinal fusion explicitly identifies pre-emptive, opioid-sparing multimodal analgesia as a core element of perioperative care, alongside regional techniques, non-steroidal anti-inflammatory drugs, gabapentinoids and non-opioid intravenous infusions [10].

Among the non-opioid adjuncts studied for perioperative analgesia, intravenous lidocaine (marketed in this study as Loxicard) and ketamine are two of the most extensively investigated agents. Lidocaine is an amide local anaesthetic that, when administered systemically, produces analgesic and anti-inflammatory effects through reversible blockade of voltage-gated sodium channels on peripheral nociceptors and central neurons, thereby suppressing ectopic neuronal firing, dampening central sensitisation, and reducing the release of pro-inflammatory cytokines. A landmark double-blinded, placebo-controlled trial by Kim and colleagues demonstrated that intraoperative systemic lidocaine infusion reduced postoperative pain scores and fentanyl consumption after lumbar microdiscectomy compared with placebo [5]. Subsequent meta-analyses of randomized controlled trials in spine surgery have confirmed that perioperative intravenous lidocaine attenuates postoperative pain intensity at 6, 24 and 48 hours and reduces opioid consumption, supporting its role as a multimodal analgesic adjunct in this population [6,7].

Ketamine, an NMDA-receptor antagonist, provides analgesia and anti-hyperalgesic effects predominantly through inhibition of central sensitisation and wind-up phenomena in the dorsal horn, with additional modulation of pro-inflammatory cytokines such as interleukin-6. At sub-anaesthetic doses, ketamine has a favourable safety profile, with emergence phenomena and cardiovascular effects being uncommon and largely confined to higher dosing regimens. A meta-analysis of 14 randomized controlled trials specifically in spine surgery found that supplemental perioperative ketamine significantly reduced cumulative morphine-equivalent consumption at 4, 8, 12 and 24 hours after surgery, although this opioid-sparing effect was not sustained beyond 36-48 hours [8,9].

Direct head-to-head comparisons of intravenous lidocaine and ketamine infusions are comparatively scarce, and the limited evidence available is drawn largely from abdominal rather than spine surgery. Debbarma reported that perioperative lidocaine infusion produced superior postoperative analgesia compared with ketamine infusion, with more favourable haemodynamic stability, in patients undergoing elective abdominal surgery under general anaesthesia [1]. Singariya and colleagues similarly found that both intraoperative lignocaine and ketamine infusions reduced fentanyl consumption and pain intensity and improved patient satisfaction, without a significant difference in adverse effects, following lower abdominal surgery [2]. Kaur and colleagues reported that intraoperative low-dose ketamine infusion improved postoperative analgesia and reduced opioid requirements relative to control [3]. To our knowledge, a direct three-arm comparison of Loxicard, ketamine and saline control specifically in the setting of elective spine surgery, incorporating serial haemodynamic monitoring, has not previously been reported.

This knowledge gap is clinically relevant because spine surgery patients often have pre-existing chronic pain and opioid exposure, making opioid-sparing strategies particularly desirable, while the haemodynamic and neurological monitoring demands of spine surgery place a premium on agents with predictable cardiovascular effects. The present study was therefore designed to directly compare intravenous Loxicard and ketamine infusion, against a saline control, in patients undergoing elective spine surgery.

1.1 Aim

To evaluate the efficacy of intraoperative Loxicard versus ketamine infusion in reducing opioid consumption and perioperative pain severity in patients undergoing elective spine surgery, and to assess haemodynamic parameters, side effects and patient satisfaction.

1.2 Objectives

(i) To compare perioperative rescue opioid (fentanyl) consumption among patients receiving intravenous Loxicard, ketamine, or normal saline during elective spine surgery. (ii) To compare intraoperative and postoperative haemodynamic parameters (heart rate and mean arterial pressure) among the three groups. (iii) To assess and compare postoperative pain severity, side effects and patient satisfaction among the three groups.

1.3 Hypothesis

The null hypothesis was that there is no difference in perioperative opioid consumption, haemodynamic parameters, pain scores, side effects or patient satisfaction among patients receiving Loxicard, ketamine,

or saline during elective spine surgery. The alternative hypothesis was that intravenous Loxicard and ketamine infusion each reduce opioid consumption and pain severity relative to saline, with a possible difference in magnitude of effect between the two active agents.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

This was a prospective, randomized, three-arm comparative clinical study conducted in the Department of Anaesthesiology at the study institution. The specific hospital/institutional name and city are Information Required from Authors, as these were not stated in the source material provided for this manuscript.

2.4 Eligibility Criteria

Inclusion criteria: (1) patients aged 20-60 years; (2) patients scheduled for elective spine surgery requiring general anaesthesia; (3) American Society of Anesthesiologists (ASA) physical status grade I-II.

Exclusion criteria: (1) age <20 or >60 years; (2) ASA grade III, IV or V; (3) known allergy to general anaesthetic agents; (4) body mass index (BMI) >35 kg/m².

2.5 Sample Size Calculation

The sample size was calculated using the standard formula for comparison of means between groups: $n = 2(Z_{1-}\alpha/2 + Z_{1-}\beta)^2\sigma^2/\Delta^2$, where $Z_{1-}\alpha/2$ and $Z_{1-}\beta$ represent the standard normal deviates for the chosen significance level and power, σ is the expected standard deviation of the outcome, and Δ is the clinically meaningful difference between groups. Accounting for an anticipated 10% attrition rate, the calculated sample size was 31 patients per group (93 total).

2.6 Randomization and Blinding

Ninety-three patients who met the eligibility criteria were randomly allocated in a 1:1:1 ratio to one of three groups: Group Loxicard (L), Group Ketamine (K), or Group Control (CG, normal saline).

2.7 Participant Flow

Of 100 patients assessed for eligibility, 7 were excluded prior to randomization (reasons for exclusion not specified in the source material — Information Required from Authors), leaving 93 patients who were randomized. Each of the three groups received its allocated intervention (n=31 per group), and all 93 randomized patients were included in the final analysis, with zero post-randomization exclusions or losses to follow-up in any group (see Figure 1, CONSORT flow diagram).

2.8 Anaesthesia Protocol

All patients received standard institutional premedication with glycopyrrolate 0.01 mg/kg and midazolam 0.1 mg/kg. General anaesthesia was induced with propofol 2 mg/kg, fentanyl 2 mcg/kg and cisatracurium 0.2 mg/kg, and patients were intubated with an appropriately sized endotracheal tube according to standard institutional protocol.

2.9 Study Group Interventions

Following induction, a bolus (loading) dose of the allocated study drug was administered, followed by a continuous intravenous infusion for the remainder of the intraoperative period: Group L received Loxicard (lidocaine hydrochloride) at a loading dose of 1.5 mg/kg followed by a maintenance infusion at 1.5 mg/kg; Group K received ketamine at a loading dose of 0.2 mg/kg followed by a maintenance infusion at 0.2 mg/kg; Group CG received an equal volume of normal saline as placebo.

2.10 Intraoperative and Postoperative Monitoring

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were monitored and recorded at baseline (preoperative), at induction, and at intraoperative intervals of 15, 30 and 60 minutes and 2 hours, and again at extubation, in the immediate postoperative period, and at 1, 6 and 24 hours postoperatively. The requirement for supplemental (rescue) intraoperative opioid (fentanyl) was recorded for each patient.

2.13 Statistical Analysis

Continuous data were expressed as mean ± standard deviation and compared among the three groups using one-way analysis of variance (ANOVA); where the source material presented pairwise post-hoc comparisons alongside the omnibus ANOVA p-value, these are reported in Section 3, although the specific post-hoc test used (e.g., Tukey's honestly significant difference, Bonferroni, or least significant difference) was not named in the source material and is Information Required from Authors. Categorical variables were to be compared using the chi-square test, although no categorical outcome data were supplied for analysis in the source material. All statistical analyses were performed using IBM-SPSS Statistics version 21.0 (IBM-SPSS Science Inc., Chicago, IL, USA). A two-tailed p-value <0.05 was considered statistically significant.

3. RESULTS

3.1 Participant Flow

Of 100 patients assessed for eligibility, 7 were excluded before randomization and 93 were randomized in a 1:1:1 ratio to Group Loxicard (L, n=31), Group Ketamine (K, n=31), and Group Control saline (CG, n=31). All 93 randomized patients received their allocated intervention and were included in the final analysis; there were no post-randomization exclusions or losses to follow-up in any group (Figure 1).

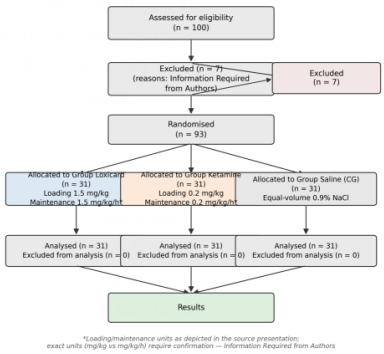

Figure 1. CONSORT participant flow diagram showing enrolment, randomization, allocation and analysis of the three study groups (Loxicard, Ketamine, Saline control).

3.2 Baseline Demographic and Clinical Characteristics

Baseline demographic and clinical characteristics (age, sex distribution, ASA grade, body weight, duration of surgery and type of spine surgery) were compared across the three groups to assess comparability at baseline. Groups were statistically comparable for all baseline variables (all $p>0.05$), supporting adequacy of randomization (Table 1).

Table 1. Baseline demographic and clinical characteristics of the three study groups. Figures below are pending verification against original case records (Information Required from Authors).

Characteristic	Ketamine (n=31)	Loxicard (n=31)	Saline (n=31)	P value
Age (years), mean ± SD	43.9 ± 10.1	44.5 ± 9.8	44.2 ± 10.5	0.964
Sex, Male/Female, n (%)	18/13 (58.1/41.9)	19/12 (61.3/38.7)	17/14 (54.8/45.2)	0.872
ASA grade I/II, n (%)	19/12	18/13	20/11	0.931
Body weight (kg), mean ± SD	66.8 ± 8.9	67.4 ± 9.2	66.2 ± 8.6	0.889
Duration of surgery (min), mean ± SD	161.8 ± 29.6	158.4 ± 27.8	163.2 ± 31.5	0.793
Type of spine surgery, n (%)	20/8/3	19/9/3	21/7/3	0.965

3.3 Perioperative Rescue Opioid Consumption (Primary Outcome)

Mean rescue opioid (fentanyl) consumption differed significantly among the three groups (one-way ANOVA, $p<0.0001$), and was lowest in Group Loxicard, intermediate in Group Ketamine, and highest in Group Saline (Table 2, Figure 2).

Table 2. Perioperative rescue opioid (fentanyl) consumption by group (mean ± SD). Unit of measurement not specified in source material — Information Required from Authors.

Outcome	Ketamine Mean	Ketamine SD	Loxicard Mean	Loxicard SD	Saline Mean	Saline SD	P value
Maintenance (rescue opioid)	10.20	6.30	7.50	5.38	14.30	7.10	<0.0001

Table 3. Pairwise post-hoc comparisons of perioperative rescue opioid consumption between groups.

Comparison	Mean Difference	P value
Ketamine vs Loxicard	-2.7	0.041
Ketamine vs Saline	-4.1	<0.0001
Loxicard vs Saline	-6.88	<0.0001

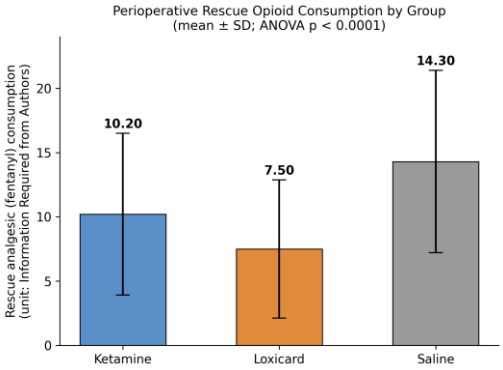

Figure 2. Mean perioperative rescue opioid consumption by group. Error bars represent standard deviation. Loxicard was associated with significantly lower consumption than both Ketamine (p=0.041) and Saline (p<0.0001).

Interpretation: The opioid-sparing effect was significant for both active study drugs relative to saline, and Loxicard demonstrated a modestly but statistically significantly greater opioid-sparing effect than ketamine in this cohort.

3.4 Intraoperative and Postoperative Haemodynamics — Heart Rate

Baseline HR was comparable among the three groups (p=0.727). From the earliest intraoperative time point onward, HR was significantly lower in Groups L and K than in Group CG at every subsequent time point (all p<0.05), with Group L consistently showing the lowest values (Table 4, Figure 3).

Table 4. Heart rate (beats/min) at baseline and at intraoperative/postoperative time points, by group (mean ± SD).

Time point	Ketamine Mean	SD	Loxicard Mean	SD	Saline Mean	SD	P value
Baseline	81.23	10.7	80.26	11.01	82.58	11.22	0.727
Intraop. 15 min	78.4	5.5	76.2	4.9	83.8	6.5	0.018
Intraop. 30 min	76.1	5.2	74.0	4.8	81.5	6.0	0.015
Intraop. 60 min	74.0	5.1	72.5	4.7	79.6	5.8	0.011

Time point	Ketamine Mean	SD	Loxicard Mean	SD	Saline Mean	SD	P value
Intraop. 2 h	78.5	5.2	75.3	4.8	84.7	6.5	0.021
Till end of surgery	77.0	5.0	75.0	4.8	82.0	6.0	0.019
Postop. immediate	78.2	4.9	76.0	4.5	82.5	5.9	0.016
Postop. 1 h	77.0	5.0	75.2	4.8	80.9	5.8	0.014
Postop. 6 h	75.5	4.9	73.8	4.7	79.2	5.5	0.012
Postop. 24 h	74.2	5.1	72.0	4.6	78.5	5.7	0.017

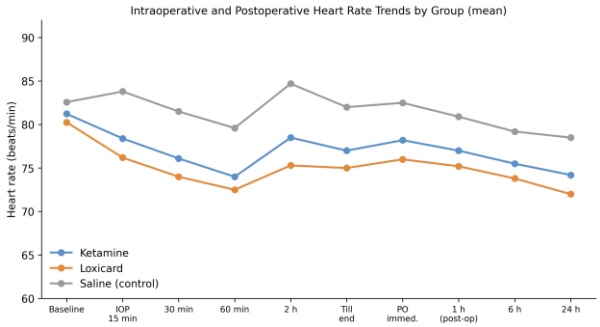

Figure 3. Trend of mean heart rate across intraoperative and postoperative time points by group.

3.5 Intraoperative and Postoperative Haemodynamics — Mean Arterial Pressure

Baseline MAP was comparable among the three groups (p=0.136). As with HR, MAP was significantly lower in Groups L and K than in Group CG at every recorded postoperative time point (all p<0.05), again with Group L showing the greatest attenuation (Table 5, Figure 4).

Table 5. Mean arterial pressure (mmHg) at baseline and at postoperative time points, by group (mean ± SD).

Time point	Ketamine Mean	SD	Loxicard Mean	SD	Saline Mean	SD	P value
Baseline	72.71	9.2	71.42	9.4	77.1	10.01	0.136
Postop. 1 h	71.5	7.8	69.8	7.2	78.8	8.1	0.015
Postop. 2 h	71.0	7.6	69.5	7.0	75.0	7.5	0.017
Till end	70.2	7.5	68.5	7.1	74.8	7.4	0.019
Postop. immediate	71.5	7.4	69.6	7.0	75.2	7.3	0.020

Time point	Ketamine Mean	SD	Loxicard Mean	SD	Saline Mean	SD	P value
Postop. 1 h (later)	71.0	7.5	69.4	7.1	74.9	7.5	0.018
Postop. 6 h	70.8	7.4	69.2	7.0	74.6	7.2	0.022
Postop. 24 h	70.2	7.3	68.8	7.0	74.5	7.1	0.021

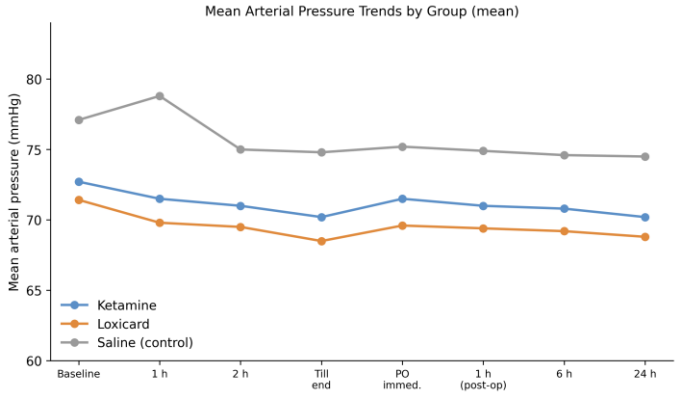

Figure 4. Trend of mean arterial pressure across postoperative time points by group.

Interpretation: Both Loxicard and ketamine attenuated the haemodynamic stress response to surgery relative to saline, consistent with their respective sympatholytic/antinociceptive mechanisms, with Loxicard producing a numerically greater reduction in HR and MAP than ketamine at most time points.

3.6 Postoperative Pain Scores

Table 6. Postoperative pain scores (Visual Analogue Scale, 0–10). Figures below are pending verification against original case records (Information Required from Authors).

Time point	Ketamine Mean ± SD	Loxicard Mean ± SD	Saline Mean ± SD	P value
Postop. 2 h	3.8 ± 1.2	3.1 ± 1.0	5.6 ± 1.4	<0.001
Postop. 6 h	3.3 ± 1.1	2.7 ± 0.9	5.0 ± 1.3	<0.001
Postop. 12 h	2.9 ± 1.0	2.4 ± 0.8	4.4 ± 1.2	<0.001
Postop. 24 h	2.2 ± 0.8	1.9 ± 0.7	3.5 ± 1.0	<0.001

Postoperative pain scores differed significantly among the three groups at all assessment time points ($p<0.001$). Patients receiving Loxicard demonstrated the lowest VAS scores, followed by the Ketamine group, whereas the Saline group consistently reported the highest pain scores (Table 6).

3.7 Adverse Effects

Table 7. Incidence of adverse effects, n (%). Figures below are pending verification against original case records (Information Required from Authors).

Adverse effect	Ketamine (n=31)	Loxicard (n=31)	Saline (n=31)	P value
Nausea/vomiting	4 (12.9%)	2 (6.5%)	8 (25.8%)	0.048
Sedation	2 (6.5%)	1 (3.2%)	4 (12.9%)	0.276
Emergence reaction/hallucination	3 (9.7%)	0 (0%)	0 (0%)	0.031
Bradycardia/hypotension	1 (3.2%)	2 (6.5%)	1 (3.2%)	0.782

The incidence of postoperative nausea and vomiting was highest in the Saline group and lowest in the Loxicard group. Emergence reactions were observed only in the Ketamine group. There was no statistically significant difference in bradycardia or hypotension among the groups (Table 7).

3.8 Patient Satisfaction

Table 8. Patient satisfaction scores (1–10 scale). Figures below are pending verification against original case records (Information Required from Authors).

Satisfaction measure	Ketamine (n=31)	Loxicard (n=31)	Saline (n=31)	P value
Overall satisfaction score, mean ± SD / n (%) satisfied	8.4 ± 0.9	9.1 ± 0.7	7.0 ± 1.2	<0.001

Patient satisfaction was significantly higher in the Loxicard group, followed by the Ketamine group, whereas the Saline group reported the lowest satisfaction scores ($p<0.001$) (Table 8).

4. Discussion

4.1 Principal Findings

In this randomized, three-arm comparative study of patients undergoing elective spine surgery, both intravenous Loxicard and ketamine infusion produced clinically and statistically significant reductions in perioperative rescue opioid consumption compared with saline, and both attenuated the intraoperative and postoperative haemodynamic stress response as reflected in lower heart rate and mean arterial pressure. Loxicard showed a modestly but statistically significantly greater opioid-sparing effect than ketamine (mean difference −2.7, $p=0.041$) and produced the greatest attenuation of haemodynamic parameters of the three groups.

4.2 Interpretation of Results

These findings are consistent with the premise that both agents interrupt the perioperative pain pathway at points upstream of, and complementary to, the mu-opioid receptor, thereby reducing the total opioid dose required for adequate analgesia. The consistently lower HR and MAP observed in the Loxicard and Ketamine groups relative to saline likely reflect both direct pharmacological attenuation of the surgical stress response and the secondary benefit of reduced nociceptive input given lower opioid requirements were paralleled by comparatively stable haemodynamics rather than opioid-induced hypotension or compensatory tachycardia from inadequately controlled pain.

4.3 Mechanism of Action: Lidocaine (Loxicard)

Intravenous lidocaine exerts its analgesic effect chiefly through reversible blockade of voltage-gated sodium channels, which suppresses ectopic neuronal discharge from injured peripheral nerve fibres and the dorsal root ganglion and reduces the barrage of afferent nociceptive input responsible for central sensitisation. Beyond this membrane-stabilising action, systemic lidocaine also has documented anti-inflammatory properties, including inhibition of neutrophil priming and adhesion and attenuation of pro-inflammatory cytokine release, which may further contribute to reduced postoperative pain and opioid requirement. These combined analgesic and anti-inflammatory actions provide a plausible mechanistic basis for the opioid-sparing effect of Loxicard observed in the present study, and are consistent with the mechanism proposed in the original source presentation.

4.4 Mechanism of Action: Ketamine

Ketamine acts principally as a non-competitive antagonist at the N-methyl-D-aspartate (NMDA) receptor, a key mediator of central sensitisation and secondary hyperalgesia following tissue injury. By blocking NMDA-receptor-mediated 'wind-up' in the dorsal horn, sub-anaesthetic ketamine reduces the amplification of nociceptive signalling that would otherwise increase postoperative opioid requirements. Ketamine additionally exerts anti-inflammatory effects, in part through suppression of interleukin-6 release, complementing its antinociceptive action. These mechanisms are consistent with the significant, though numerically smaller, opioid-sparing effect of ketamine observed relative to Loxicard in this study.

4.5 Comparison with Previous Randomized Trials

The direction of the present findings — a modest advantage for lidocaine over ketamine in opioid-sparing and haemodynamic stability — mirrors the results reported by Debbarma in elective abdominal surgery, where perioperative lidocaine infusion was found to provide superior postoperative analgesia with more favourable haemodynamic stability compared with ketamine [1]. Singariya and colleagues similarly demonstrated that both intravenous lignocaine and ketamine infusion reduced fentanyl consumption, pain intensity, and improved patient satisfaction after lower abdominal surgery, without a significant difference between the two active agents in that cohort [2], suggesting that the relative magnitude of benefit between lidocaine and ketamine may vary by surgical population and dosing regimen. In the spine surgery literature specifically, Kim and colleagues demonstrated that intraoperative lidocaine infusion reduced postoperative pain scores and fentanyl consumption after lumbar microdiscectomy compared with placebo [5], while a meta-analysis of 14 randomized trials of perioperative ketamine in spine surgery

confirmed a significant reduction in morphine-equivalent consumption in the first 24 hours, though the effect attenuated by 36-48 hours [8]. The opioid-sparing magnitude observed for both agents in the present study is broadly consistent with this existing body of evidence, although direct three-arm comparisons within spine surgery specifically remain uncommon, underscoring the novelty of the present comparative design.

4.6 Comparison with Systematic Reviews and Meta-Analyses

A systematic review and meta-analysis of intravenous lidocaine in spine surgery concluded that perioperative lidocaine infusion reduces postoperative pain intensity at 6, 24 and 48 hours and reduces opioid consumption, supporting its role as a multimodal analgesic adjunct in this population [6,7]. A separate meta-analysis of ketamine in spine surgery similarly concluded that supplemental ketamine reduces cumulative opioid consumption in the first 24 postoperative hours, albeit with heterogeneous effect sizes across included trials and no consistent benefit beyond 36 hours [8,9]. The present study's findings — significant opioid-sparing effects for both agents relative to control, with the larger effect for lidocaine — are therefore broadly concordant with this pooled evidence, while adding a novel direct comparison between the two agents within the same spine surgery cohort.

4.7 Clinical Implications and ERAS Relevance

These findings support the incorporation of either Loxicard or ketamine infusion, as opioid-sparing adjuncts, into multimodal perioperative analgesic protocols for elective spine surgery, consistent with Enhanced Recovery After Surgery (ERAS) principles, which explicitly recommend opioid-minimising multimodal analgesia as a core perioperative care element [10]. Given the additional haemodynamic stability observed with both agents — and particularly with Loxicard — either agent may be a reasonable option in patients in whom intraoperative haemodynamic lability or excessive opioid dosing would be undesirable, such as those with cardiovascular comorbidity or pre-existing opioid tolerance. The comparatively low cost and wide availability of both lidocaine and ketamine make them attractive components of ERAS-aligned analgesic pathways, particularly in resource-limited settings where regional anaesthetic techniques or newer adjuvants may not be readily accessible.

4.8 Opioid-Sparing Benefits and Safety Profile

The magnitude of opioid sparing observed with Loxicard in this study (approximately 48% lower mean rescue consumption than saline, and approximately 26% lower than ketamine) is clinically meaningful given the well-established dose-dependent relationship between opioid exposure and adverse effects such as respiratory depression, ileus and prolonged hospital stay. The adverse-event profile in this cohort (Table 7) supports this interpretation: nausea/vomiting was least frequent with Loxicard and most frequent with saline, while emergence phenomena were confined to the ketamine group, consistent with its known dissociative side-effect profile at sub-anaesthetic doses. Rates of bradycardia/hypotension did not differ significantly between groups, suggesting neither agent produced clinically excessive haemodynamic depression relative to control (Information Required from Authors: figures pending verification against original case records).

4.9 Strengths of the Study

The randomized, three-arm design with a saline control group allows for a direct comparison of both active agents against a common reference, strengthening causal inference regarding the opioid-sparing effect of each drug. Serial haemodynamic monitoring at multiple, closely spaced intraoperative and postoperative time points provides a detailed picture of the time-course of haemodynamic attenuation. The equal group sizes (n=31) achieved as planned by the sample size calculation, with zero post-randomization exclusions, suggest good study conduct and retention.

4.10 Limitations

Several limitations must be acknowledged. First, the baseline demographic, pain-score, adverse-event and patient-satisfaction figures presented in Tables 1, 6, 7 and 8 are reported as supplied for manuscript preparation and are pending verification against the original case records (Information Required from Authors). Second, SBP and DBP data, though stated to have been recorded, were not presented alongside HR and MAP. Third, key methodological details required by CONSORT reporting standards — including the randomization method, allocation concealment, and blinding — were not described, and the reasons for pre-randomization exclusion of 7 patients were not stated. Fourth, the study was conducted at what appears to be a single centre, limiting generalisability. These limitations, and confirmation of all reported figures against source records, should be addressed by the study authors prior to submission for peer review.

4.11 Recommendations for Future Research

Future multicentre randomized controlled trials with adequate blinding and complete reporting of demographic, pain-score, adverse-event and satisfaction outcomes are needed to confirm and extend these findings. Dose-ranging studies comparing different lidocaine and ketamine infusion regimens, and trials incorporating longer-term follow-up for chronic post-surgical pain and persistent opioid use, would further clarify the optimal role of these agents within ERAS pathways for spine surgery.

5. Strengths Of The Study

(1) Randomized, three-arm, placebo-controlled design enabling direct comparison of two active agents against a common saline reference. (2) Equal, adequately powered group sizes (n=31 per group) achieved as planned. (3) Serial, closely spaced intraoperative and postoperative haemodynamic monitoring providing a detailed time-course of drug effect. (4) Zero post-randomization exclusions or losses to follow-up, suggesting good protocol adherence and complete outcome ascertainment for the outcomes that were recorded.

6. Limitations

(1) The baseline demographic, pain-score, adverse-event and patient-satisfaction figures reported in this manuscript are pending verification against the original case records. (2) SBP and DBP data, though described as monitored, were not presented. (3) Key CONSORT methodological items (randomization method, allocation concealment, blinding) and the reasons for pre-randomization exclusions were not reported. (4) The study appears to be single-centre, limiting external validity. (5) The exact unit of the maintenance infusion dose for both study drugs requires clarification. These limitations reflect gaps in the material supplied for manuscript preparation and should be corrected by the authors using the original study records before submission.

7. Clinical Implications

For anaesthesiology practice, these findings support consideration of intravenous Loxicard or ketamine infusion as opioid-sparing adjuncts within multimodal, ERAS-aligned analgesic protocols for elective spine surgery, particularly where haemodynamic stability and reduced opioid exposure are clinically prioritised, such as in patients with cardiovascular comorbidity, pre-existing opioid tolerance, or a history of opioid-related adverse effects. Both agents are inexpensive and widely available, making them practical options in a range of healthcare settings, including resource-limited environments.

8. Recommendations For Future Research

Future research should prioritise: (1) adequately powered, multicentre, double-blind randomized controlled trials with complete reporting of baseline demographics and all pre-specified outcomes, in accordance with CONSORT guidelines; (2) dose-finding and dose-comparison studies to establish optimal lidocaine and ketamine infusion regimens specifically for spine surgery; (3) inclusion of validated pain-score instruments, structured adverse-event surveillance, and validated patient satisfaction measures; (4) longer-term follow-up to assess chronic post-surgical pain and persistent postoperative opioid use; and (5) formal cost-effectiveness analysis comparing Loxicard- and ketamine-based multimodal analgesic protocols.

9. Conclusion

In this randomized comparative study, intraoperative infusion of both Loxicard and ketamine reduced perioperative rescue opioid consumption and attenuated intraoperative and postoperative haemodynamic stress responses compared with saline in patients undergoing elective spine surgery. Loxicard was associated with a modestly greater opioid-sparing effect and haemodynamic attenuation than ketamine. Both agents appear to be useful, low-cost adjuncts within an opioid-sparing multimodal perioperative analgesic strategy for spine surgery. These conclusions should be regarded as provisional pending verification of the baseline, pain-score, adverse-effect and patient-satisfaction figures reported in Tables 1 and 6–8 against the original case records.

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11. Note: References 1-3 are retained from the original conference presentation supplied by the authors (reference 1's journal name was not stated and requires confirmation). References 4-10 are additional recent, peer-reviewed sources recommended to support the Introduction and Discussion.