Section: Anaesthesiology

Original Research Article

KETAMINE AS AN ADJUNCT TO INTERSCALENE BLOCK FOR SHOULDER ARTHROSCOPY: A RANDOMIZED, DOUBLE-BLIND, CONTROLLED TRIAL

Aravind B Guledagudd[1], Arun A Bevoor[2], Sukanya Mitra[3], Arushi Goyal[4]

[1]*DM Resident, Department of Critical Care Medicine, Bangalore Medical College and Research Institute, Bengaluru, Karnataka 560002, India.*
[2]*Assistant Professor, Department of Anaesthesiology, S. Nijalingappa Medical College and HSK Hospital, Bagalkot, Karnataka 587102, India.*
[3]*Professor, Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Sector 32, Chandigarh 160030, India.*
[4]*Anaesthetics Fellow, Royal Liverpool University Hospital, United Kingdom.*

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Corresponding Author:
Dr. Aravind B Guledagudd,
DM Resident, Department of Critical Care Medicine, Bangalore Medical College and Research Institute, Bengaluru, Karnataka 560002, India.
Email: aravindbg2012@gmail.com

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ABSTRACT

Background: Interscalene block (ISB) is the standard technique for postoperative analgesia after arthroscopic shoulder surgery, and ketamine, an N-methyl-D-aspartate receptor antagonist, has been used as an opioid-sparing analgesic adjunct. **Objectives:** To evaluate the effect of low-dose intravenous ketamine, added to ultrasound-guided continuous interscalene block (CISB) with patient-controlled regional analgesia (PCRA), on the duration and quality of postoperative analgesia after arthroscopic shoulder surgery.

Material and Methods: In this prospective, randomized, double-blind, controlled trial, sixteen adults undergoing arthroscopic shoulder surgery under general anaesthesia combined with ultrasound-guided CISB were randomized to intravenous ketamine (bolus 0.35 mg/kg, infusion 0.5 mg/kg/hour; Group I, n=8) or an equivalent volume of normal saline (Group II, n=8). Time to first PCRA bolus (primary outcome) was analysed by the Kaplan-Meier method and log-rank test; secondary outcomes were compared using Student's t-test, the Mann-Whitney U test, or two-way repeated-measures ANOVA, as appropriate.

Results: Time to first PCRA bolus was longer with ketamine (963.75 ± 41.46 minutes) than with saline (809.37 ± 48.80 minutes; $p<0.001$). Group I required fewer analgesic boluses (23.25 ± 2.25 vs 28.50 ± 1.19; $p<0.001$), consumed less total analgesic solution (116.25 ± 11.25 vs 142.50 ± 5.97 mL; $p<0.001$), and reported higher satisfaction scores (87.50 ± 1.85 vs 83.50 ± 2.61; $p=0.003$) than Group II. No adverse effects occurred in either group.

Conclusion: Low-dose intravenous ketamine, combined with ultrasound-guided continuous interscalene block and PCRA, prolongs postoperative analgesia, reduces analgesic consumption, and improves satisfaction after arthroscopic shoulder surgery, without adverse effects.

Keywords: Ketamine; Nerve Block; Analgesia, Patient-Controlled; Arthroscopy; Shoulder.

INTRODUCTION

Effective regional anaesthesia techniques reduce side effects and analgesic requirements, reduce pain intensity, and improve patient comfort by blunting the neuroendocrine response to surgery, thereby reducing postoperative opioid requirements. Peripheral nerve blocks (PNBs) also reduce postoperative nausea and vomiting and may shorten the time to functional recovery.[1]

Interscalene block (ISB) is considered the gold-standard block for postoperative analgesia after shoulder surgery. Pain after arthroscopic shoulder surgery can be disproportionately severe relative to

the size of the surgical incision, reflecting the extensive intra-articular and capsular soft-tissue manipulation involved, and inadequately controlled early pain may delay mobilization and rehabilitation; combining general anaesthesia with regional analgesia reduces intraoperative anaesthetic requirements and improves postoperative pain control.[2] ISB provides excellent intraoperative anaesthesia and muscle relaxation for outpatient shoulder arthroscopy without the need for high-dose intravenous opioids or paralytics,[3] and can be administered as either a continuous or single-injection technique.[2]

Ultrasound guidance (USG) improves visualization of brachial plexus anatomy and block localization.[4] USG-guided ISB improves block onset, quality, and success while reducing the mean effective anaesthetic concentration and volume required,[5] and is associated with a higher success rate, shorter procedure time, fewer needle passes, and faster onset compared with nerve-stimulator-guided techniques.[6] USG-guided ISB also has a lower rate of conversion to general anaesthesia, reduces the local anaesthetic volume and intraoperative analgesic or sedative requirements compared with non-ultrasound techniques, and has been associated with fewer complications such as vessel puncture or nerve injury.[7] Ultrasound guidance also improves safety by reducing the risk of local anaesthetic systemic toxicity (LAST).[5]

Patient-controlled analgesia (PCA) allows patients autonomy in timing small doses of analgesic or local anaesthetic as required, and is used in both parenteral and regional analgesic techniques.[8] Continuous PNB confers greater patient satisfaction, fewer systemic opioid side effects, faster recovery, and earlier ambulation.[9,10]

Many local anaesthetics, alone or combined with adjuncts, have been used to prolong postoperative analgesia with limited success.[11,12] Ketamine, an old phencyclidine-analogue dissociative anaesthetic used clinically since 1970, acts by blocking the N-methyl-D-aspartate (NMDA) receptor and has more recently been studied as an opioid-sparing adjunct to reduce opioid-related side effects such as constipation, confusion, pruritus, nausea, vomiting, and urinary retention. Subanaesthetic doses have been used in severe depression and chronic pain, and, as an adjunct, in acute pain; recent guidelines underscore the perioperative opioid-sparing efficacy of low-dose intravenous ketamine.[13]

Few studies have examined the role of perioperative intravenous ketamine combined with continuous interscalene block for postoperative analgesia after arthroscopic shoulder surgery.[14,15] The present study aimed to evaluate the postoperative analgesic-sparing effect of low-dose intravenous ketamine combined with continuous interscalene block using patient-controlled regional analgesia (PCRA).

MATERIALS AND METHODS

This prospective, randomized, double-blind, controlled trial was conducted in the Department of Anaesthesia and Intensive Care, Government Medical College and Hospital, Chandigarh, in collaboration with the Department of Orthopaedics. After approval from the Institutional Ethics Committee (GMC/IEC/2018/217) and registration with the Clinical Trials Registry of India (CTRI/2019/05/018898), and after obtaining written informed consent, patients undergoing shoulder surgery were screened against the following eligibility criteria.

Inclusion Criteria

- American Society of Anesthesiologists (ASA) physical status I–II
- Age 18–65 years
- Body mass index (BMI) 18–30 kg/m² of either sex
- Arthroscopic shoulder surgery, specifically rotator-cuff repair or surgery for recurrent shoulder dislocation

Exclusion Criteria

- Refusal of informed consent
- History of relevant drug allergy
- History of psychiatric illness or substance abuse
- Severe cardiovascular, respiratory, metabolic, or neurological disease
- Pregnancy or lactation
- Coagulopathy
- Contralateral phrenic nerve dysfunction
- Infection at the planned injection site
- Use of α2-agonists for hypertensive disorders
- Current steroid therapy

Sample size

Sample size was estimated from a published study that used ketamine as an adjunct to lidocaine in supraclavicular block, in which time to first request for supplementary analgesia was 8.93 hours (SD 1.0) with ketamine-lidocaine versus 7.3 hours (SD 1.93) with lidocaine alone ($p<0.001$).[16] Using these data with an alpha of 0.05 and power of 90%, the estimated sample size was 19 per group; a sample of 20 per group was therefore planned to be adequately powered.

Randomization and study groups

Forty patients were originally planned for random allocation; however, because of disruption to elective surgical services during the COVID-19 pandemic, only sixteen patients could be enrolled and were randomized, using a computer-generated random-number table with sequentially numbered, sealed, opaque envelopes, to one of two groups:

- **Group I (n=8):** intravenous ketamine, pre-incisional bolus 0.35 mg/kg, and intraoperative infusion 0.5 mg/kg/hour.[13]
- **Group II (n=8):** normal saline in a volume equivalent to the ketamine bolus and infusion.

Both the patient and the assessing investigator were blinded to group allocation. The study drug was

prepared by a person not otherwise involved in the study, in unlabelled, identical-looking syringes, and handed to the anaesthesiologist performing the block by a person not involved in the study or its assessments. Patient flow through screening, randomization, allocation, follow-up, and analysis is summarized in the CONSORT diagram (Figure 1), in accordance with the CONSORT 2010 Statement for reporting randomized trials.[17]

Anaesthetic and block technique

Before surgery, all patients underwent a complete work-up and pre-anaesthetic evaluation, and were counselled, in their own language, on the use of PCRA, the categorical nausea scale (0, none; 1, mild; 2, moderate; 3, severe), the linear visual analogue scale (VAS) for pain (0, no pain; 10, worst imaginable pain), and the manual muscle test (MMT: 0, no palpable or observable contraction; 1, palpable or observable contraction without motion; 2, moves without gravity through full range of motion; 3, moves against gravity through full range of motion; 4, moves against gravity and moderate resistance through full range of motion; 5, moves against gravity and maximal resistance through full range of motion with flexion and extension of the fingers and wrist).[18] Patients fasted for a minimum of six hours and received tablet alprazolam 0.25 mg and tablet ranitidine 150 mg orally on the night before and on the morning of surgery.

The block was performed in the operating room with the patient's head elevated and rotated away from the operative side, after skin preparation with 10% povidone-iodine and local infiltration with 2% lidocaine. Standard monitoring (electrocardiogram, pulse oximetry, and non-invasive blood pressure) was established, and an intravenous infusion of normal saline (2 mL/kg/hour) was commenced through an 18G cannula.

The brachial plexus is formed by the ventral rami of C5–C8 and T1, which unite into superior, middle, and inferior trunks; divide into anterior and posterior divisions; and reorganize into lateral, posterior, and medial cords that give rise to the terminal nerves supplying the upper limb. [Image 1]

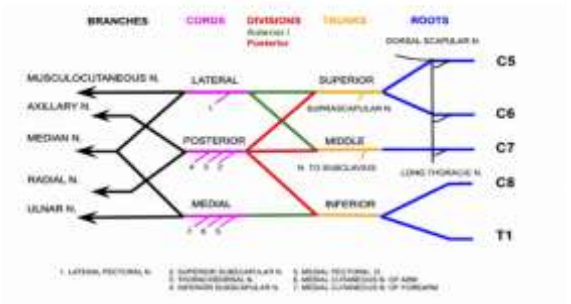

Image 1: Line diagram of the brachial plexus, illustrating its roots, trunks, divisions, cords, and terminal branches.

A high-frequency (5–10 MHz) ultrasound probe was placed transversely at the level of the cricoid cartilage and moved laterally to identify the carotid artery, internal jugular vein, and, more laterally, the anterior and middle scalene muscles. The roots of the brachial plexus were identified between these muscles as three hypoechoic vesicles lying in close proximity — the so-called "traffic-light sign" (Image 2).

Image 2: Ultrasound image at the level of the cricoid cartilage showing the roots of the brachial plexus (C5–C7) as three hypoechoic vesicles lying between the anterior scalene muscle (ASM) and middle scalene muscle (MSM) — the "traffic-light sign".

Under continuous in-plane ultrasound guidance, a 19G needle was advanced anteriorly toward the brachial plexus, passing between the anterior and middle scalene muscles, and generalized shoulder contractions were sought at a stimulating current below 0.5 mA (Image 3).

Image 3: Ultrasound-guided in-plane needle placement for continuous interscalene block, showing the needle tip advancing toward the C6–C7 roots of the brachial plexus between the scalene muscles.

A bolus of 20 mL of 0.5% ropivacaine with 4 mg perineural dexamethasone was then given under ultrasound guidance in both groups to establish the block (time zero). A 20G catheter was threaded through the needle 5 cm beyond the needle tip; the needle was withdrawn over the catheter, and the catheter was secured on the contralateral shoulder with a transparent dressing.

Sensory block was assessed every two minutes for ten minutes by loss of sensation to pinprick over the deltoid using a three-point scale (0, normal sensation; 1, sharp to pinprick; 2, pinprick felt but not sharp; 3, no sensation), and motor block by failure to abduct the shoulder — the "deltoid sign" (0, normal abduction; 1, decreased but present abduction; 2, unable to abduct). General anaesthesia was then induced with intravenous glycopyrrolate 0.2 mg, fentanyl 2 µg/kg, propofol 2 mg/kg, and vecuronium 0.1 mg/kg, and maintained with isoflurane (0.5–2%) in nitrous oxide/oxygen (60:40).[19] Supplemental fentanyl (1 µg/kg) was permitted for a 20% rise above baseline haemodynamic parameters.

Group I received the intravenous ketamine bolus after induction and before incision, followed by the intraoperative infusion, stopped 15 minutes before the anticipated end of surgery; Group II received an equivalent-volume saline bolus and infusion on the same schedule. Ondansetron 0.1 mg/kg was given to all patients 15 minutes before completion of surgery, and residual neuromuscular block was reversed with neostigmine 50 µg/kg and glycopyrrolate 10 µg/kg before extubation.

In the post-anaesthesia care unit, the perineural catheter was connected to a PCRA pump (0.2% ropivacaine with fentanyl 2 µg/mL) delivering 5 mL patient-controlled boluses with a 30-minute lockout interval. The number of boluses and any adverse effects were recorded, and a satisfaction score was obtained at the end of the 48-hour study period.

Data collection and outcome measures:

Patients were monitored for 48 hours after the block. Morphometric and demographic characteristics were recorded at enrolment, and heart rate, electrocardiogram, oxygen saturation, end-tidal carbon dioxide, and respiratory rate were monitored continuously. Postoperatively, pain (VAS, at rest and on movement), nausea (categorical scale), and MMT score were assessed; nausea or vomiting was treated with intravenous metoclopramide 10 mg. The primary outcome was time to first PCRA bolus (a marker of duration of analgesia). Secondary outcomes were VAS pain scores over 48 hours (at 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 30, 36, 42, and 48 hours), total analgesic consumption, patient-satisfaction score (0–100 VAS at 48 hours), and adverse effects.

Statistical analysis:

Data were analysed using SPSS version 17.0 (SPSS Inc., Chicago, IL). The primary outcome — time from adequate sensory block to first PCRA bolus — was analysed by Cox regression and the Kaplan-Meier method, with groups compared by the log-rank test. Continuous variables were tested for normality with the Kolmogorov-Smirnov test. Single time-point, between-group comparisons used Student's t-test (normally distributed continuous variables), the Mann-Whitney U test (non-normally distributed continuous variables), the chi-square test (binary variables), or the Wilcoxon test (ordered categorical variables). Repeated-measures data (pain scores, sensory/motor scores, heart rate, and blood pressure over time) were analysed by two-way repeated-measures ANOVA with post-hoc Scheffé's test. Significance was set at $p<0.05$.

RESULTS

Sixteen patients (eight per group) completed the 48-hour study protocol; enrolment was terminated before the planned sample of forty patients was reached because elective shoulder arthroscopy was suspended for part of the study period during the COVID-19 pandemic. There were no losses to follow-up, protocol discontinuations, or exclusions after randomization. [Figure 1]

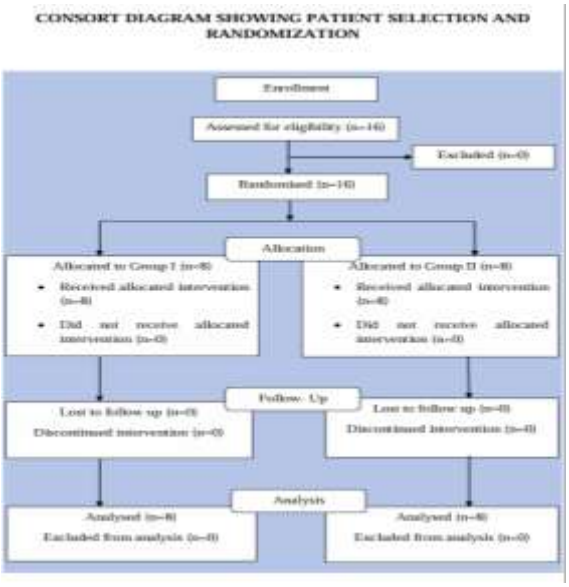

Figure 1: CONSORT flow diagram showing patient screening, randomization, allocation, follow-up, and analysis. All sixteen randomized patients (eight per group) completed follow-up and were included in the analysis, with no losses to follow-up, protocol discontinuation, or exclusions

Baseline characteristics

The two groups were comparable at baseline. There were no significant differences in age, weight, height, or BMI (Table 1). Group I comprised seven males and one female, and Group II six males and two females; five patients in Group I and six in Group II were ASA physical status I, and the remainder were ASA physical status II. Preoperative haemoglobin, total leucocyte count, fasting blood glucose, blood urea nitrogen, and serum creatinine, as well as baseline heart rate, respiratory rate, and systolic and diastolic blood pressure, were also similar between groups (all $p>0.05$; Table 1).

Table 1: Baseline Demographic, Clinical, and Haemodynamic Characteristics of the Two Groups

Parameter	Group I (n=8)	Group II (n=8)	P Value
Age (years)	35.12 ± 13.94	32.25 ± 9.19	0.634
Weight (kg)	66.00 ± 6.82	68.37 ± 5.15	0.445
Height (cm)	166.37 ± 4.27	166.00 ± 4.75	0.871
BMI (kg/m²)	23.79 ± 1.81	24.84 ± 1.51	0.229
Sex, male/female	7/1	6/2	—
ASA status, I/II	5/3	6/2	—
Haemoglobin (g/dL)	13.78 ± 1.37	12.95 ± 1.42	0.265
Total leucocyte count (cells/mm³)	7750.0 ± 977.0	7350.0 ± 1318.0	0.502
Fasting blood sugar (mg/dL)	98.50 ± 2.97	96.62 ± 5.68	0.422
Blood urea nitrogen (mg/dL)	26.37 ± 1.40	25.87 ± 2.99	0.676
Serum creatinine (mg/dL)	0.73 ± 0.14	0.82 ± 0.11	0.197
Baseline heart rate (bpm)	81.37 ± 7.30	81.25 ± 6.22	0.971
Baseline respiratory rate (/min)	16.37 ± 0.74	16.62 ± 0.51	0.448
Baseline systolic BP (mmHg)	122.75 ± 10.41	126.25 ± 7.88	0.461
Baseline diastolic BP (mmHg)	71.50 ± 2.77	72.00 ± 3.85	0.770

Data are mean ± SD unless otherwise stated. ASA = American Society of Anesthesiologists physical status; BMI = body mass index; BP = blood pressure.

Block and intraoperative characteristics

Sensory block onset was faster with ketamine than with saline (2.25 ± 0.46 vs 2.75 ± 0.46 minutes; p=0.049); motor block onset, MMT recovery at 2, 5, and 10 minutes, and duration of surgery did not differ significantly between groups. [Table 2]

Table 2: Interscalene Block and Intraoperative Characteristics

Parameter	Group I (n=8)	Group II (n=8)	P Value
Sensory block onset (min)	2.25 ± 0.46	2.75 ± 0.46	0.049
Motor block onset (min)	4.75 ± 0.46	4.88 ± 0.35	0.554
MMT score at 2 min	2.75 ± 0.46	3.00 ± 0.75	0.438
MMT score at 5 min	1.63 ± 0.51	1.88 ± 0.64	0.405
MMT score at 10 min	0.00 ± 0.00	0.00 ± 0.00	—
Duration of surgery (min)	70.00 ± 28.28	75.00 ± 25.63	0.717

Data are mean ± SD. MMT = manual muscle test.

Postoperative haemodynamics and oxygenation

Arterial oxygen saturation remained stable in both groups and did not differ significantly at any of the fifteen postoperative time points assessed over 48 hours (all p>0.05; Table 3). Postoperative heart rate, respiratory rate, and systolic and diastolic blood pressure likewise showed no significant between-group differences at any time point, intraoperatively or postoperatively (all p>0.05; detailed values available from the corresponding author on request).

Table 3: Postoperative Arterial Oxygen Saturation (SpO_2, %) Over 48 Hours

Time (h)	Group I (n=8)	Group II (n=8)	P Value
4	100.00 ± 0.00	99.87 ± 0.35	0.334
6	99.75 ± 0.46	99.75 ± 0.70	1.000
8	98.62 ± 0.91	99.12 ± 0.99	0.312
10	98.87 ± 0.99	99.25 ± 0.70	0.398
12	98.87 ± 0.83	99.12 ± 0.83	0.559
14	99.12 ± 0.83	98.87 ± 0.64	0.513
16	99.25 ± 0.88	99.00 ± 0.75	0.554
18	99.37 ± 0.51	99.50 ± 0.75	0.705
20	98.87 ± 0.83	99.25 ± 0.70	0.349
22	98.37 ± 0.91	99.25 ± 0.88	0.073
24	98.75 ± 0.70	99.00 ± 0.75	0.506
30	99.12 ± 0.83	98.62 ± 1.06	0.312
36	99.25 ± 0.70	99.00 ± 1.06	0.590
42	99.37 ± 0.91	99.50 ± 0.75	0.770
48	99.37 ± 0.74	99.75 ± 0.46	0.246

Data are mean ± SD.

Primary outcome — duration of analgesia

Time to first PCRA bolus, the primary outcome, was significantly longer in Group I than in Group II (963.75 ± 41.46 vs 809.37 ± 48.80 minutes; log-rank $\chi 2=16.72$, p<0.001; Figure 2, Table 4).

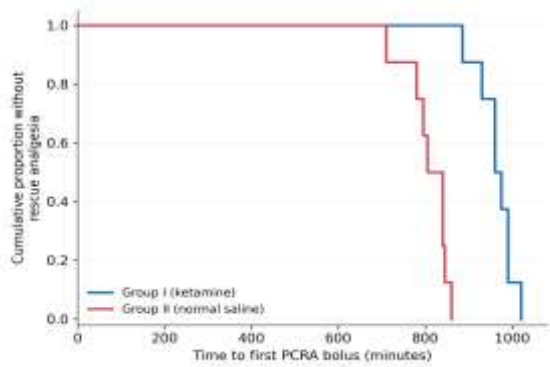

Figure 2: Kaplan-Meier curve showing the cumulative proportion of patients without rescue analgesia after ultrasound-guided continuous interscalene block. Patients receiving intravenous ketamine (Group I) required significantly longer time to first PCRA bolus than those receiving normal saline (Group II) (log-rank p<0.001).

Secondary outcomes

Group I self-administered fewer analgesic boluses over 48 hours than Group II (23.25 ± 2.25 vs 28.50 ± 1.19; p<0.001) and consumed less total analgesic solution (116.25 ± 11.25 vs 142.50 ± 5.97 mL; p<0.001), and reported a higher satisfaction score at 48 hours (87.50 ± 1.85 vs 83.50 ± 2.61; p=0.003; Figure 4, Table 4).

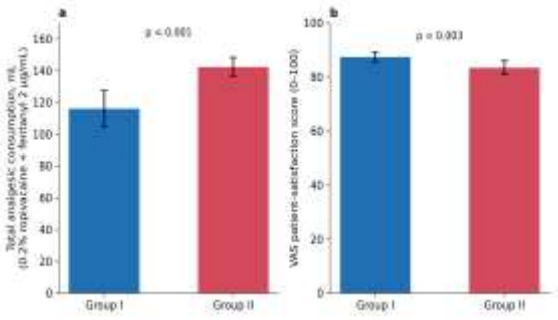

Figure 4: (a) Total postoperative analgesic (0.2% ropivacaine with fentanyl 2 µg/mL) consumption and (b) VAS patient-satisfaction score at 48 hours in Group I (ketamine) and Group II (normal saline). Error bars represent standard deviation.

Table 4: Primary and Secondary Analgesic Outcomes

Parameter	Group I (n=8)	Group II (n=8)	P Value
Time to first PCRA bolus (min)	963.75 ± 41.46	809.37 ± 48.80	<0.001
Total analgesic boluses over 48 h	23.25 ± 2.25	28.50 ± 1.19	<0.001
Total analgesic consumption (mL)*	116.25 ± 11.25	142.50 ± 5.97	<0.001
VAS satisfaction score (0–100)	87.50 ± 1.85	83.50 ± 2.61	0.003

*Data are mean ± SD. PCRA = patient-controlled regional analgesia; VAS = visual analogue scale. *0.2% ropivacaine with fentanyl 2 µg/mL.*

VAS pain scores at rest (Figure 3a) differed significantly between groups at 16 hours (lower in Group I; 1.87 ± 1.64 vs 3.62 ± 0.91; p=0.020), 20 hours (higher in Group I; 3.62 ± 0.91 vs 2.62 ± 0.51; p=0.018), and 24 hours (lower in Group I; 2.37 ± 0.74 vs 3.12 ± 0.64; p=0.049), but not at the remaining twelve time points. On two-way repeated-measures ANOVA, the main effect of group was not significant (F=2.89, p=0.091), the main effect of time was significant (F=35.98, p<0.001), and the group×time interaction was significant (F=2.52, p=0.002), consistent with a differential, non-monotonic pattern of pain relief between groups over the observation period.

VAS pain scores on movement (Figure 3b) differed significantly between groups only at 14 hours (lower in Group I; 1.00 ± 0.92 vs 3.00 ± 2.07; p=0.026). On two-way repeated-measures ANOVA, the main effect of group was significant in favour of Group I (F=4.86, p=0.029), the main effect of time was significant (F=40.56, p<0.001), and the group×time interaction was significant (F=2.01, p=0.018).

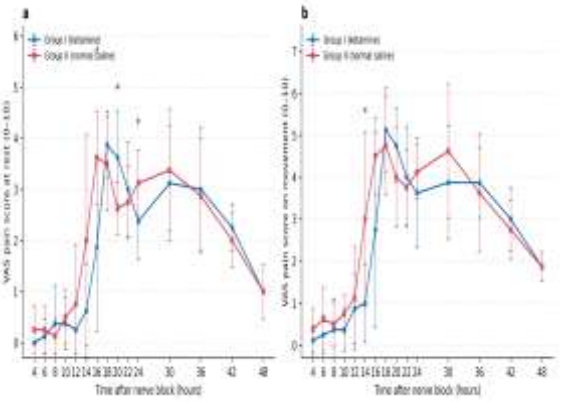

Figure 3: Mean (±SD) visual analogue scale (VAS) pain scores (a) at rest and (b) on movement over the 48-hour postoperative period in Group I (ketamine) and Group II (normal saline). Asterisks denote time points with statistically significant between-group differences (p<0.05).

Adverse effects

No adverse effects, including nausea, vomiting, sedation, bradycardia, Horner's syndrome, or catheter-related complications, occurred in either group.

DISCUSSION

This randomized, double-blind trial found that low-dose intravenous ketamine, added to ultrasound-guided continuous interscalene block with PCRA, significantly prolonged the time to first rescue analgesic bolus, reduced 48-hour analgesic consumption, and improved patient satisfaction after arthroscopic shoulder surgery, without increasing adverse effects.

The trial enrolled sixteen of the forty patients originally planned, because recruitment of elective arthroscopic shoulder surgery patients was interrupted during the COVID-19 pandemic. The mean age was 35 years in Group I and 32 years in Group II; eleven of the sixteen patients were ASA physical status I and five were ASA physical status II.

We are not aware of directly comparable trials using an identical perineural-catheter technique with ultrasound-guided ISB, although several studies have examined ketamine as an analgesic adjunct in regional anaesthesia more broadly. Our primary-outcome finding is consistent with that of Brinck et al,[20] who reported that perioperative intravenous ketamine prolongs the time to first postoperative analgesic request. In the present study, the difference in mean time to first bolus between groups was 154.38 minutes, considerably longer than the roughly 38-minute difference reported by Brinck et al,[20] which may reflect the addition of 4 mg perineural dexamethasone to the block solution used here in both groups.

In a recent systematic review and meta-analysis of twenty studies of low-dose ketamine in orthopaedic surgery, Riddell et al,[21] found a significant reduction in total opioid consumption and a longer time to first postoperative opioid request with ketamine, together with improved pain scores at 24 and 48 hours; however, in the arthroscopic-surgery subgroup specifically, the effect on opioid use and pain scores was equivocal. Our findings — a longer time to first bolus and reduced analgesic consumption with ketamine — are therefore more favourable than the pooled arthroscopy-subgroup estimate in that review, possibly reflecting differences in ketamine dose, block technique, or the concomitant use of perineural dexamethasone.

Woo et al,[14] used a similar bolus-and-infusion ketamine regimen (0.3 mg/kg and 0.15 mg/kg/hour) added to single-shot ISB after arthroscopic shoulder surgery and found no reduction in early pain scores or prolongation of time to first analgesic request; they attributed this null result to the use of 5 mg dexamethasone as an adjuvant in both study groups, which may have equally prolonged analgesia in both arms and obscured any effect of ketamine. In the present study, both the ketamine bolus (0.35 mg/kg) and infusion (0.5 mg/kg/hour) doses were higher, which may have contributed to the more clearly demonstrable benefit observed here despite dexamethasone being included in the block solution for both groups.

The pattern of VAS pain scores at rest showed a significant group×time interaction without a significant overall main effect of group, with the ketamine group scoring lower at 16 and 24 hours but higher at 20 hours; this oscillating pattern is compatible with a delayed peak in breakthrough pain in the ketamine group around the time its longer block was finally wearing off, while the saline group — whose block wore off earlier — had already been receiving regular PCRA top-ups by this point. On movement, by contrast, the main effect of group favoured ketamine, suggesting a more consistent benefit for pain provoked by activity than for pain at rest.

The opioid- and local-anaesthetic-sparing effect of ketamine observed in this trial is consistent with its pharmacological profile as a non-competitive NMDA-receptor antagonist. NMDA-receptor activation at the spinal dorsal horn contributes to "wind-up" and central sensitization following surgical tissue injury, and subanaesthetic ketamine is thought to attenuate this process, thereby reducing the perceived intensity of postoperative pain and delaying the need for rescue analgesia independent of any direct action on the peripheral nerve block itself,[13] This mechanistic distinction may help explain why a benefit of ketamine was still apparent well after the local anaesthetic component of the block — identical in both groups — would ordinarily have worn off, and is in keeping with the rationale for using ketamine as a systemic adjunct rather than as a substitute for regional blockade.

No adverse effects or catheter-related complications were observed in either group, consistent with the generally favourable safety profile of low-dose ketamine reported in previous reviews.[21]

Strengths

This trial has several methodological strengths. Treatment allocation was concealed using sequentially numbered, sealed, opaque envelopes, and both the patient and the assessing investigator were blinded to group allocation, with the study drug prepared and dispensed by personnel not otherwise involved in the study or its assessments. The primary outcome was analysed using a survival-analysis framework (Kaplan-Meier method with log-rank comparison) appropriate to a time-to-event endpoint, rather than a simple between-group mean comparison. As documented in the CONSORT flow diagram (Figure 1), all sixteen randomized patients completed the 48-hour protocol with no losses to follow-up, protocol discontinuations, or post-randomization exclusions, so the analysis is free of attrition or exclusion bias. The trial was also prospectively registered (CTRI/2019/05/018898) and approved by an institutional ethics committee before enrolment began.

Limitations

This trial has several limitations. The sample size was markedly smaller than originally planned

because of pandemic-related disruption to elective surgery, which limits statistical power, particularly for secondary and time-point-specific comparisons, and increases the chance of both false-negative and false-positive findings. The trial was conducted at a single centre, used a fixed ketamine dose without dose-ranging, and followed patients for only 48 hours, so longer-term outcomes and dose-response relationships could not be assessed. Both groups received perineural dexamethasone, which may have narrowed the observable difference between groups and limits generalisability to protocols that do not use a steroid adjuvant.

CONCLUSION

Low-dose intravenous ketamine, given as a pre-incisional bolus and intraoperative infusion alongside ultrasound-guided continuous interscalene block and PCRA, significantly prolonged the duration of postoperative analgesia and reduced analgesic consumption after arthroscopic shoulder surgery, with improved patient satisfaction and no observed adverse effects. These findings support intravenous ketamine as a useful analgesic adjunct in this setting, although confirmation in an adequately powered trial is warranted.

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Conflict of Interest: None declared.
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Ethical Statement

The study was approved by the Institutional Ethics Committee, Government Medical College and Hospital, Chandigarh (GMC/IEC/2018/217), was registered with the Clinical Trials Registry of India (CTRI/2019/05/018898), and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

REFERENCES

1. Liu SS, Strodtbeck WM, Richman JM, Wu LC. A comparison between regional and general anaesthesia for ambulatory anaesthesia: a meta-analysis of randomized controlled trials. Anesth Analg. 2005;101:1634-42.
2. Elbahrawy K, El-Deeb A. Dexamethasone versus ketamine in the interscalene block in patients undergoing arthroscopic shoulder surgery: a randomized double-blinded study. Asian J Anesthesiol. 2018;56:136-42.
3. Singh A, Kell C, O'Brien T, Wilson J, Warner J. Ultrasound-guided interscalene block anesthesia for shoulder arthroscopy. J Bone Joint Surg Am. 2012;94:2040-6.
4. Kapral S, Greher M, Huber G, Willschke H, Kettner S, Kdolsky R, et al. Ultrasonographic guidance improves the success rate of interscalene brachial plexus blockade. Reg Anesth Pain Med. 2008;33:253-8.
5. Barrington MJ, Kluger R. Ultrasound guidance reduces the risk of local anesthetic systemic toxicity following peripheral nerve blockade. Reg Anesth Pain Med. 2013;38:289-99.
6. Lim JA, Sung SY, Lee JH, Lee SY, Kwak SG, Ryu T, et al. Comparison of ultrasound-guided and nerve stimulator-guided interscalene blocks as a sole anesthesia in shoulder arthroscopic rotator cuff repair: a retrospective study. Medicine (Baltimore). 2020;99:e21684.
7. Soeding PE, Sha S, Royse CE, Marks P, Hoy G, Royse AG. A randomized trial of ultrasound-guided brachial plexus anaesthesia in upper limb surgery. Anaesth Intensive Care. 2005;33:719-25.
8. Ilfeld BM, Vandenborne K, Duncan PW, Sessler DI, Enneking FK, Shuster JJ, et al. Ambulatory continuous interscalene nerve blocks decrease the time to discharge readiness after total shoulder arthroplasty: a randomized, triple-masked, placebo-controlled study. Anesthesiology. 2006;105:999-1007.
9. Aguirre J, Del Moral A, Cobo I, Borgeat A, Blumenthal S. The role of continuous peripheral nerve blocks. Anesthesiol Res Pract. 2012;2012:1-20.
10. Chavan SG, Koshire AR, Panbude P. Effect of addition of fentanyl to local anesthetic in brachial plexus block on duration of analgesia. Anesth Essays Res. 2011;5:39-42.
11. Ullah H, Samad K, Khan FA. Continuous interscalene brachial plexus block versus parenteral analgesia for postoperative pain relief after major shoulder surgery. Cochrane Database Syst Rev. 2014;2:CD007080.
12. Cummings KC 3rd, Napierkowski DE, Parra-Sanchez I, Kurz A, Dalton JE, Brems JJ, et al. Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine. Br J Anaesth. 2011;107:446-53.
13. Schwenk ES, Viscusi ER, Buvanendran A, Hurley RW, Wasan AD, Narouze S, et al. Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Reg Anesth Pain Med. 2018;43:456-66.
14. Woo JH, Kim YJ, Baik HJ, Han JI, Chung RK. Does intravenous ketamine enhance analgesia after arthroscopic shoulder surgery with ultrasound-guided single-injection interscalene block? A randomized, prospective, double-blind trial. J Korean Med Sci. 2014;29:1001-6.
15. Lee IO, Kim WK, Kong MH, Lee MK, Kim NS, Choi YS, et al. No enhancement of sensory and motor blockade by ketamine added to ropivacaine interscalene brachial plexus blockade. Acta Anaesthesiol Scand. 2002;46:821-6.
16. Rahimzadeh P, Faiz SH, Ziyaeifard M, Niknam K. Effectiveness of adding ketamine to ropivacaine infusion via femoral nerve catheter after knee anterior cruciate ligament repair. J Res Med Sci. 2013;18:632-6.
17. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c332.
18. Byeon GJ, Shin SW, Yoon JU, Kim EJ, Baek SH, Ri HS. Infusion methods for continuous interscalene brachial plexus block for postoperative pain control after arthroscopic rotator cuff repair. Korean J Pain. 2015;28:210-6.
19. Patel HH, Pearn ML, Patel PM, Roth DM. General anesthetics and therapeutic gases. In: Brunton LL, Hilal-Dandan R, Knollmann BC, editors. Goodman & Gilman's the Pharmacological Basis of Therapeutics. 13th ed. New York: McGraw Hill; 2018. p.387-404.
20. Brinck ECV, Tiippana E, Heesen M, Bell RF, Straube S, Moore RA, et al. Perioperative intravenous ketamine for acute postoperative pain in adults. Cochrane Database Syst Rev. 2018;12:CD012033.
21. Riddell JM, Trummel JM, Onakpoya IJ. Low-dose ketamine in painful orthopaedic surgery: a systematic review and meta-analysis. Br J Anaesth. 2019;123:325-34.