



## POST OPERATIVE ANALGESIC EFFECTS WITH LOW DOSE OF INTRAVENOUS KETAMINE IN LOWER LIMB BELOW KNEE ORTHOPAEDIC SURGERIES DURING SPINAL ANESTHESIA- A RANDOMIZED CLINICAL TRIAL

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### ABSTRACT

**Objective:** The aim of our study is to find the effect of low-dose intravenous ketamine on postoperative pain and the need for supplemental analgesics following lower limb below knee orthopaedic surgeries under spinal anesthesia using heavy bupivacaine

**Materials and methods:** After ethical committee approval and written informed consent, 60 patients of age group 20 to 45 years of both sex and ASA I to II undergoing surgeries for below knee orthopaedic procedures were randomly allocated into two groups of 30 patients each. After administration of spinal anaesthesia with 3cc of 0.5% heavy bupivacaine in both group, Group K receives ketamine (0.25 mg/kg) with 1 mg midazolam & Group P receives Normal saline with 1 mg midazolam. Patient with failed spinal are excluded from the study. The Numerical rating pain scale will be compared between 2 groups at the time intervals 0,1,2,3,4,5,6,7,8,12. Primary outcome duration of analgesia & secondary outcome – Total doses of rescue analgesic requirements postoperatively.

**RESULTS:** Duration of analgesia was significantly higher in ketamine group ( $380.2 \pm 48.2$  min) compared to placebo group ( $144.4 \pm 16$  min). (P-value <0.001) Total analgesic dose was significantly lower in ketamine group ( $112 \pm 33$ mg) compared to placebo ( $212 \pm 33$ mg). (P-value <0.001)

**Conclusion:** We conclude that administration of low doses of ketamine after spinal anesthesia prolong the duration of analgesia and reduces the total doses of rescue analgesic requirements postoperatively

**KEYWORDS :** Intravenous Ketamine, orthopaedic surgeries

### INTRODUCTION:

Postoperative pain produce physical, cognitive, and emotional discomfort to the patients. It lead to serious consequences such as impaired wound healing and rehabilitation, delayed gastrointestinal motility, pulmonary complication, higher risk of thromboembolism due to immobilization, and myocardial ischemia. Adequate and proper management of the pain could improve the quality of life of the patients.

Intravenous low dose Ketamine- sub anaesthetic dose has a good analgesic effects & which had been used for postoperative pain relief. It has been considered a good substitute for opioids for controlling postoperative pain

### AIM OF THE STUDY:

The aim of our study is to find the effect of low-dose intravenous ketamine on postoperative pain and the need for supplemental analgesics following lower limb below knee orthopaedic surgeries under spinal anesthesia using heavy bupivacaine

### MATERIALS AND METHODS:

This study was carried out in Kanyakumari government medical college hospital orthopaedic surgery theatre after institutional ethical committee approval and this study is to find the effect of low dose ketamine in lower limb below knee orthopaedic surgeries under spinal anesthesia using heavy bupivacaine and written informed consent.

Randomized prospective control clinical trial studied for a period of 3 months with 60 patient with ASA physical status I, II, III patients coming for Lower limb below knee surgeries randomised into two groups group (K, P) - 30 patients each, Group K-ketamine (0.25 mg/kg) with 1 mg midazolam in 5 milliter syringe and group P - Normal saline with 1 mg midazolam in 5 milliliter syringe

**INCLUSION CRITERIA:** Age 20-45 yrs, ASA I, II, III, Written informed consent

**EXCLUSION CRITERIA:** Patient's refusal, ASA 4, Cardiac disease, H/o Head trauma- ICH, Drug addiction, psychiatric drugs usage,

hallucination, delirium, Coagulation abnormality/ thrombocytopenia, Failed Spinal

### RANDOMIZATION: CLOSED ENVELOPE TECHNIQUE

60 plain covers each with a single sheet written K for ketamine 0.25 mg/kg with 1 mg of midazolam in 30 sheets, written P for Normal saline with 1 mg of midazolam in 30 sheets were prepared and kept in the operation theatre. The covers were mixed thoroughly. Before start of the surgery the patient picked up a cover of their choice and were randomized accordingly. Duty anaesthesiologist will prepare the drug to be given.

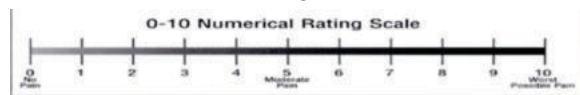
**INTERVENTION:** All patients will receive premedication with Inj. Metoclopramide & Inj. Ranitidine intravenously before shifting the patient into operating room. In the operation theatre, after securing 18-gauge cannula. Baseline cardiorespiratory parameters (non-invasive blood pressure, Pulse rate, SpO<sub>2</sub> and electrocardiogram) were recorded using Anaesthesia monitor- Philips sure sign. Blood pressure is measured in the Right upper arm. Subarachnoid block is performed in the sitting position under aseptic precautions. A 25 gauge spinal needle (Quincke's) was inserted in the L3-4 interspace and 3 ml (15mg) of hyperbaric (0.5%) Bupivacaine. All patients sedated with 1 mg of midazolam. Inj ketamine and placebo given 10 min after spinal anaesthesia according to the groups.

### BLINDING:

Double blinded both the patient and observer are blinded

### OBSERVATION:

The Numerical rating pain scale will be compared at the time intervals 0,1,2,3,4,5,6,7,8,12 during rest.



Inj. TRAMADOL 100mg was given intramuscularly when Numerical rating scale score  $\geq 4$  and the time will be noted as time of first analgesic dose. Duration of analgesia is defined as the time interval between the administration of drug or normal saline

and the time of first analgesic dose.

**PARAMETERS MONITORED**

- Demographic data - Age.
- Sensory block – By spirit cotton-able to perceive cold sensation at 1 min after spinal anaesthesia
- Blood pressure and pulse rate
- Numerical pain scale for 12 hrs postoperatively
- Duration of analgesia
- Complications if any

**OUTCOME**

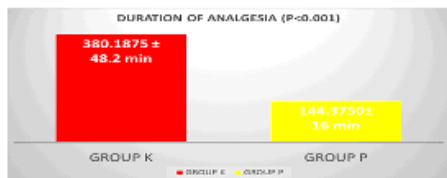
**Primary outcome** - Duration of analgesia -Time interval between the drug administration and the time of first analgesic dose. **Complications** - Nausea, vomiting, hallucination. **Secondary outcome**- Total doses of rescue analgesic requirement postoperatively.

**SAMPLING:**

Sample size calculation was performed from the previous study “Small Dose Ketamine Improves Postoperative Analgesia and Rehabilitation after Total Knee Arthroplasty” published in *Anesth Analg.* 2005 Feb; 100(2): 475–480. doi: [10.1213/ 01.ANE.00001 42117.82241.DC. Twenty five patients per group thus provided an 80% power for detecting a 40% difference in opioid consumption at an alpha level of 0.05

**RESULTS:**

The observations are tabulated and analysed statistically using SPSS statistical package Version 23.



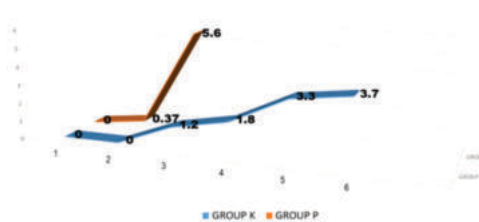
Total Resue analgesics dose (Pvalue <0.001)



**TABLES**

	Duration of Analgesia		Total dose of rescue Analgesia	
	MEAN	SD	MEAN	SD
GROUP K	380.18	48.17	112 mg	34 mg
GROUP P	144.37	16.0	212 mg	34 mg
P VALUE	<0.001		<0.001	

MEAN VAS SCORES IN HOURS



**DISCUSSION:**

In our study duration of analgesia was significantly higher in ketamine group (380.2 ± 48.2 min) compared to placebo group (144.4 ± 16 min). (P-value <0.001). Total analgesic dose was significantly lower in ketamine group (112 ± 34mg) compared to placebo (212 ± 34mg). (P-value <0.001). NRS scale score was significantly lesser in ketamine group from 3<sup>rd</sup> hour onwards. Sen et al.,s study confirmed the effect of preemptive ketamine [with spinal

bupivacaine] on pain relief (VAS) too, and also illustrated “low dose ketamine (0.15 mg) could reduce the need for analgesia” [during 24 after the operation]. Bauchat and colleagues examined the effect of intravenous ketamine 10mg administered during spinal anaesthesia for cesarean delivery on the incidence of breakthrough pain, the pain that required supplemental postoperative analgesia. Arbabi and Ghazi-Saidi also reported less severe pain in women who received low-dose ketamine for postoperative pain following caesarean section

A Cochrane database review evaluating the postop analgesic effectiveness of ketamine, reported that perioperative ketamine reduces postop opioid requirements and reduces PONV. The primary mechanism of its analgesic and anaesthetic effects on the central nervous system and spinal cord receptors resembles NMDA receptor antagonism.ketamine oxidases via microsomal enzyme system and it metabolizes into 80% of nor-ketamine. 5% of ketamine also reduces to of hydroxy-ketamine. Nor-ketamine is an analgesic molecule that is as effective as 20-30% of ketamine . Nor-ketamine continues to exist longer than 5 hours after the application. This fact may explain the continued significantly low scores of pains after the 3rd hours in our study. Analgesic effects includes supraspinal effects, suppression of central sensitization, a phenomenon by which dorsal root neurons increase their spontaneous discharge rate, responsiveness and enlarge their receptive field in response to repeated painful stimulus

**COMPLICATIONS:**

None of the patients were registered complications like Nausea, Vomiting, Hallucination etc. during the study period. Similar to our study,Meer et al. reported that ketamine in anesthesia for cesarean section had lower side effects. Candrakartan suggested that the reason that ketamine decreases PONV incidence can be its opioid sparing effect in his recent review

**CONCLUSION:**

We conclude that administration of low doses of ketamine after spinal anaesthesia prolong the duration of analgesia and reduces the total doses of rescue analgesic requirements postoperatively. It is recommended that due to significant postoperative pain relief without considerable side effects, ketamine in low dosage (less than 1 mg/kg) might be useful.

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