

# Ketamine Wound Infiltration For Postoperative Pain Management: A Placebo Double Blinded Controlled Study.

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#### ABSTRACT

**Background.** Ketamine has been used for different purposes however its use by infiltration for management of postoperative pain is not common in this sub region, hence the need for this study. The aim of the present study was to evaluate the efficacy of infiltration of ketamine on postoperative pain relief afterabdominal surgeries done under general anesthesia...

**Methods.** After ethical approval**Eighty two patients** between the ages of 18 and 60 years being planned for abdominal surgeries were randomized and enrolled for the procedure. Patients were divided into two groups: group A had subcutaneous infiltration of 2ml/kg of ketamine diluted to 10mls at the site of incision immediately after the surgery before dressings while group B had equal volume of **normal saline infiltrated at the line of incision.** Visual analog scale (VAS) values and analgesic consumption were evaluated for 24 hours after operation.

**Results.** VAS scores were significantly lower at arrival to the post anesthesia care unit, 15, 30 and sixty minutes in the recovery room and also within the twenty four hours of surgery with the B maintaining higher VAS score and analgesic consumption in the recovery room minute (P < 0.05). The time to first analgesic request was longer in A while the frequency of analgesics was higher in group B.

**Conclusion.** A 2 mg/kg dose of subcutaneous infiltration at the end of surgery provides an adjunctive analgesia during 24 hours after surgery in patients undergoing elective abdominal surgeries.

KEYNOTES: Ketamine, infiltration, abdominal surgeries, postoperative pain

## I. INTRODUCTION

Postoperative pain is one of the most undesirable experiences for a patient undergoing surgery. Deliberate action should be taken to prophylactically treat the pain. If postoperative pain does develop, it should be managed early and aggressively, because severe pain induces a delay in discharge and poorer patient satisfaction.

One of important factors in patient recovery is postoperative analgesia. Although many studies <sup>1</sup> confirmed that effective analgesia decreases postoperative complications, pain often is overlooked and its control unsatisfactory <sup>2</sup>. Releases of proteolytic and inflammatory mediators after surgical trauma generate powerful nociceptive impulses that trigger pain <sup>3</sup>.

The most important phenomenon in transmission of inflammatory pain is sensitization of spinal cord with active contribution of glutamate and aspartate amino acids on the N-methyl-dimethyl-aspartate receptors (NMDA)<sup>4</sup>.

Ketamine, a non-competitive NMDA antagonist, prevents central sensitization of nociceptors at sub anesthetic doses by elimination of peripheral afferent noxious stimulation <sup>5-7</sup>. Stubhaug et al.<sup>8</sup> showed that ketamine decreases acute postoperative pain by inhibiting C-fiber activity.

Ketamine has been in use as an induction anaesthetic agent in our environment. Its analgesic property is not much utilized except in burns unit where it is sometimes used for wound dressings. This study aims at exploring the analgesic property of ketamine by wound infiltration.

## II. METHODOLOGY

This randomized double blinded study was conducted on Eighty twopatients ASA 1 to III who were planned for abdominal surgeries after obtaining cosecant from them and ethical approval



from the ethical committee of the hospital. The study was carried out at LAUTECH Teaching Hospital Osogbo and Ogbomoso between May 2021 and November 2022.

INCLUSSION CRITERIA Patients within ages 18 to 60 and ASA physical status Ito III that consented to the study, EXCLUSSION CRITERIA

Patients with chronic pain

Patients that reacts to Ketamine or has history of anaphylaxis

Patient with significant cardiac or respiratory illness

Patient with psychiatric illness or that could not understand the VAS method of pain assessment after proper education.

The patients were randomized into two groups A and B using computer generated table of random numbers, all in a sealed opaque envelopes in box. Patients after consenting to the study were made to pick from the envelopes without replacement.

All patients were admitted a day before surgery and were reviewed generally and systemically. Baseline investigations including Packed Cell Volume, Electrolytes urea and creatinine. Chest X ray (if more than 40 years) were done. Blood were grouped and cross matched or saved depending on the Packed Cell Volume and the risk of transfusion. All patients were premedicated with tab diazepam 10 mg to allay anxiety and metoclopramide 10mg to assist gastric emptying and reduce risk of postoperative vomiting. All patients preoperatively were taught how to evaluate their acute pain intensity using a visual analog scale (VAS) scored from 0 to 10 where 0 = no pain and 10 = the worst pain imaginable and were fasted overnight

On the morning of surgery, patients were brought to the theatre. Preanaestheticcheckup was done for the equipment and drugs were withdrawn and labelled inside syringes. Intravenous assess was established for the patient and multipara meter machine was attached to record the baseline vital signs.

Patients were induced with intravenous propofol 2mg/Kg and intubated with 1mg/Kg of suxamethonium and appropriate size endotracheal tube. Appropriate tube placement were ascertained with bilateral auscultation and capnograph. Patients were thereafter maintained on inhalational halothane and pancuronium at 0.1mg/Kg.

At the end of surgery before wound dressings drugs in the syringes labelled A and B were taken from a senior registrar who prepared them and were handed over to the surgeons in a sterile manner who in turn infiltrated the wounds. . Inhalational agent were cut off and patients were reversed with atropine 0.04 mg/Kg and neostigmine 0.05 mg/Kg.

Patients were then taken to postoperative room where postoperative monitoring and management continued. Time to first analgesic request were recorded in the postoperative room. Analgesia were maintained with diclofenac 75mg 12hourly and Intravenous Paracetamol 600mg 8 hourly. Pentazocine 30mg were given intravenously as rescue analgesic on demand when the Visual Analogue Scale was more than 3.Time to first analgesic request, VAS score at first analgesic request and the total analgesic( pentazocine consumption were noted in the first 24 hours postoperatively though patients were discharged to the ward when stable at the recovery room.

TABLE I: SOCIODEMOGRAPHIC CHARACTERISTICS				
VARIABLE		GROUP A	GROUP B	P Value
AGE		$48.6 \pm 10.2$	$52.6 \pm 9.6$	0.24
SEX		16:16	14:18	0.12
WEIGHT		68.8±12.4	76.2±10.2	
DURATION	OF	90± 12.2	$88.4 \pm 11.4$	0.84
SURGERY				

III. RESULTS



## TABLE 11 TIME TO FIST ANALGESIC REQUEST, VAS AT FIRST ANALGESIC REQUEST FREQUENCY AND TOTAL ANALGESIC CONSUMPTION

VARIABLE	GROUP A	GROUP B	P VALUE
Time to first analgesic	$15.4{\pm}1.4$	150.6±7.9	0.001
request(mins)			
VAS at first analgesic	8.6±0.45	4.2±0.28	0.04
request			
Frequency of rescue	3.2±0.22	0.16±0.18	0.002
analgesic			
Total analgesic	88.8±12.4	10.4±2.2	0.001
consumption (mg)			

TABLE III: NO OF PATIENTS REQUIRING RESCUE ANALGESICS

NO	OF	PATIENTS	WITH	38(95)	2(5)
RESCUE ANALGESIC					

## TABLE IV INCIDENCE OF NAUSEA AND VOMITING

	CDOUD ANN (0/)	CDOUDDN(0)
	GROUP ANN (%)	GROUP B N (%)
NAUSEA	1 (2.5)	5 (12.5)
VOMITING	0	2 (5)

## TABLE VAVERAGE SEDATION SCALES

	GROUP A	GROUP B
Average sedation scale N $\pm$ SD	1.4±0.4	$3.6 \pm 0.4$

It is important to state that out of the eighty two patients recruited for the study, data from two of the patients were discarded. One of the patients had difficult intubation that warranted second dose suxamethonium which might affect unset of pain postoperatively. The other patient patient had intraoperative event that warranted invitation of other specialties, had a prolonged surgery and was admitted postoperatively into the intensive care unit. Hence data from eighty patients were analyzed.

Both groups were demographically similar as shown in table 1. Time to first analgesic request was prolonged in the ketamine group with p value of 0.001 with VAS score at the first analgesic higher in the Saline group 8.6 vs. 4.2 with p value of 0.02, Frequency of analgesics were higher in the saline group while the pentazocine consumption was also higher in the saline group Table 11.

Five (5) percent of the patients in the Ketamine group had rescue analgesic (pentazocine) while Ninety five (95) percent of the saline group had pentazocine as rescue analgesic Table III

In terms of side effects/complications more patients in the Ketamine group with Nausea (5vs1) and vomiting (2vs1) which is not significant (Table IV), the two patients that had vomiting were treated with 10mg metoclopramide. Patients in the Ketamine group maintained a higher average sedation scores (3.8vs 1.4) but none was deeply sedated to warrant intensive care admission. (Table V)

## IV. DISCUSSION

Our results demonstrated that the postoperative wound infiltration with ketamine decreases postoperative pain scores without significant side effects.

We also confirmed that a ketamine infiltration also delays the time to first request for analgesic and produces a significant petazocine sparing effect and reduction in consumption during the first 24 hours.

The result of this study is in keeping with that done by Abd EL-Rahman and El Sherif<sup>8</sup>, who concluded that local wound instillation of ketamine reduced total postoperative morphine consumption and delayed the first request of rescue analgesia,

Mohamed et al.<sup>9</sup> concluded that local wound infiltration with 2 mg/kg ketamine added to bupivacaine had an opioid-sparing effect, delayed the first request of rescue analgesia, and attenuated postoperative stress response. Also Rhaman et al.<sup>10</sup> reported that SC ketamine infiltration at a dose of 2 mg/kg given approximately 15 minutes before surgical incision provided adjunctive analgesia for 24 h after surgery and related that to the local effect of ketamine.



Alex Oham<sup>11</sup> in this sub region also found out that ketamine infiltration prolongs the analgesic time of bupivacaine infiltration in children that underwent inguinal hernioraphy. The study being done in this sub regionsubstantiated the analgesic potency of ketamine infiltration. Semangin<sup>12</sup> et al in a metaanalysis found out that ketamine as adjuvant in series of blocks prolonged period of analgesia. Also El Sheriff<sup>13</sup> et al in their study found out that ketamine infiltration provides postoperative analgesia and also reduces the production of inflammatory mediators. Although this study did not set out to evaluate the effects of ketamine on production of inflammatory mediators our study is in agreement with that of El Sheriff. Othman et al. [20] who added 1mg/kg ketamine to modified pectoral block, increased time to the first request of analgesic requirement in the 1<sup>st</sup> 48 hrs. postoperatively and reduced the total morphine consumption.

All the studies were in agreement with our study with regards to analgesic activity of subcutaneous ketamine.

Our study found out a little higher incidence of nausea and vomiting and mild to moderate sedation in ketamine group which is also in agreement with above studies.

## V. CONCLUSSION

Ketamine wound infiltration has been found to have analgesic potential with little insignificant incidences of Nausea, vomiting and sedation.

Recommendations

Ketamine wound infiltration is advised to reduce the incidence and severity of postoperative pain.

To reduce incidence of nausea and vomiting an antiemetic is advisable prophylactically before wound infiltration with Ketamine.

## LIMITATION

Post-operative assessment of pain severity with VAS was of difficulty as the cognitive functions of patients is required to characterize their pain and as such VAS score assessment were with some difficulties in the early postoperative period.

CONFLICT OF INTREST None.

## REFRENCES

[1]. A. Johansen, L. Romundstad, C. S. Nielsen, H. Schirmer, and A. Stubhaug, "Persistent postsurgical pain in a general population: prevalence and predictors in the Tromso study," Pain, vol. 153, no. 7, pp. 1390–1396, 2012.

- M Suzuki, "Role of N-methyl-D-aspartate receptor antagonists in postoperative pain management," Current Opinion in Anaesthesiology, vol. 22, no. 5, pp. 618– 622, 2009. View at: <u>Publisher</u> Site | Google Scholar
- [3]. S. Himmelseher and M. E. Durieux, "Ketamine for perioperative pain management," Anesthesiology, vol. 102, no. 1, pp. 211–220, 2005.
- [4]. Abd EL-Rahman, A. and El Sherif, F. (2018) Efficacy of Postoperative Analgesia of Local Ketamine Wound Instillation Following Total Thyroidectomy; A Randomized, Double-Blind, Controlled Clinical Trial. The Clinical Journal of Pain, 34, 53-58.
- [5]. Mohamed, S., Sayed, D., El Sherif, F. and Abd El-Rahman, A.M. (2018) Effect of Local Wound Infiltration with Ketamine versus Dexmedetomidine on Postoperative Pain and Stress after Abdominal Hysterectomy, a Randomized Trial. European Journal of Pain, 22, 951-960. https://doi.org/10.1002/ejp.1181
- [6]. Safavi, M., Honarmand, A. and Nematollahy, Z. (2011) Pre-Incisional Analgesia with Intravenous or Subcutaneous Infiltration of Ketamine Reduces Postoperative Pain in Patients after Open Cholecystectomy: A Randomized, Double-Blind, Placebo-Controlled Study. Pain Medicine, 12, 1418-1426.https://doi.org/10.1111/j.1526-4637.2011.01205.x
- Javid, M., Rahimi, M. and Keshvari, A.
   (2011) Dissociative Conscious Sedation, an Alternative to General Anesthesia for Laparoscopic Peritoneal Dialysis Catheter Implantation: A Randomized Trial Comparing Intravenous and Subcutaneous Ketamine. Peritoneal Dialysis International, 31, 308-314. <u>https://doi.org/10.3747/pdi.2010.00110</u>
- [8]. Othman, A., Abd El Rahman, A. and El Sherif, F. (2016) Efficacy and Safety of Ketamine Added to Local Anesthetic in the Modified Pectoral Block for Management of Postoperative Pain in Patients Undergoing Modified Radical Mastectomy. Pain Physician, 19, 485-494. <u>https://doi.org/10.36076/ppj/2016.19.485</u>
- [9]. MohammedrizaSafavi, AzimHonarmand, Zarah Nematollahy. Pre-Incisional



Analgesia with Intravenous or Subcutaneous Infiltration of Ketamine Reduces Postoperative Pain in Patients after Open Cholecystectomy: A Randomized, Double-Blind, Placebo-Controlled Study. Pain Medicine, Volume 12, Issue 9, September 2011, Pages 1418– 1426

- [10]. Md. Pervez Rahman1. A.B.M ShafiulAnam. Rafigul Md. Islam Pre-Operative Effectiveness of Subcutaneous Infiltration of Ketamine for Post-Operative Analgesia and Haemodynamic Attenuation. KYAMC Journal Vol. 12, No. 1, April 2021.
- [11]. <u>Alex Oham<sup>1</sup>, Ifeoma Ekwere<sup>1</sup>, Kingsley</u> <u>Tobi</u>. Subcutaneous ketamine prolongs the analgesic effect of local infiltration of plain Bupivacaine in children undergoing inguinal herniotomy. Afr Health Sci. 2020 Jun;20(2):806-814
- [12]. <u>SemagnMekonnen</u> <u>Abate</u>,GetachewMergia, SolomonNega. Efficacy and safety of wound infiltration modalities for postoperative pain management after cesarean section: a systematic review and network metaanalysis protocol. Systematic Reviews.2022. 11, Article number: 194
- [13]. <u>Fatma A. El Sherif<sup>1</sup>, Moaaz Tohamy<sup>1\*</sup>, Mohamed A. M. Mostafa<sup>1</sup>, Suzanne de la Adlan<sup>2</sup>. Effect of Local Wound Infiltration with Ketamine versus Dexmedetomidine Added to Bupivacaine on Inflammatory Cytokines, a Randomized Clinical Trial<u>Open Journal of Anesthesiology</u>. 2022; Vol.12 No.8</u>