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LIDOCAINE VS KETAMINE INFUSION IN POSTOPERATIVE ANALGESIA IN ELECTIVE ABDOMINAL SURGERIES UNDER GENERAL ANAESTHESIA: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT **Background:** There is evidence that perioperative intravenous ketamine and lidocaine reduce postoperative pain, postoperative analgesic uses and improve quality of recovery. But there is limited experience and experiment in this part of India. The aim of this study was to evaluate the effect of lidocaine and ketamine on postoperative outcomes in patients undergoing elective abdominal surgeries under general anaesthesia. **Methods:** A placebo controlled RCT was conducted among 60 patients (1:1:1) at a tertiary care hospital, Tripura during 2020- 2021. After appropriate intervention, data were analysed using SPSS 21.0 and appropriate statistical test was applied. Trail was registered. **Results:** The mean age of the participants was 42.35 ± 7.22 years with comparable gender, religion and body weight distribution. Lower bispectrality Index score shows with lignocaine (78.80±3.122) at 40-60 mg of dose compare to other interventions (p-0.001). Study shows better haemodynamic control postoperatively with lidocaine than ketamine. Group L required only 2 doses of inj. diclofenac in the first 24 hours but other study groups received more than two doses as analgesia. group L has better pain control and physical comfort with a p value of 0.02 and 0.01 respectively than group K and group C which was found to be statistically significant. **Conclusion:** Postoperative outcome was better with lidocaine that ketamine among abdominal surgery cases. Further multi-centric studies with larger sample controlling the confounders can be conducted.

KEYWORDS : Lidocaine, ketamine, post-operative pain, efficacy, BIS.

INTRODUCTION

Maintaining adequate depth of anaesthesia in the intraoperative period is considered as one of the main components or points of anaesthesiology.[1] Incidence of recall and awareness under general anaesthesia has been reported to be between 0.2% to 1.6%.[2] When intraoperative awareness occurs, the patient can have devastating psychological and cognitive effects. Bispectral Index Score (BIS) monitoring and Electroencephalography (EEG) are the most commonly used monitoring for depth of anaesthesia. BIS value of 100 indicates the patient is fully awake, on the other hand BIS value of 0 indicates the absence of brain activity. [3,4] Perioperative effects of intravenous lidocaine infusion were evaluated in several animal studies showing a reduction of minimum alveolar concentration (MAC) of volatile anaesthetics and intraoperative opioids consumption.[5] Postoperative pain can be a mixture of inflammatory and neuropathic pain, often presenting as an increased sensitivity to pain. These are targets of i.v. lidocaine which is often use to control postoperative outcome.[5] Ketamine, a phencyclidine derivative, N-methyl-d-aspartate (NMDA) receptor antagonist which at anaesthetic dose (≥1.0 mg/kg intravenous), prolonged analgesic effect despite its short half-life and its use in sub-anaesthetic doses is theorized to be due to blockade of spinal cord central sensitization.[7] At sub-anaesthetic doses (≤0.3 mg/kg IV), ketamine possesses centrally mediated analgesic properties with minimal effects on consciousness and cognition. Numerous clinical studies support the role of sub-anaesthetic ketamine as an analgesic, particularly for acute pain in the perioperative settings.[7] Various studies have reported the anaesthetic sparing effects and post operative analgesic effects of inj. dexmedetomidine, lidocaine, ketamine infusions individually. Many studies have compared the anaesthetic sparing effects and postoperative analgesic effects of inj. dexmedetomidine and lidocaine infusions.[8] But very few studies have compared the effects of the two drugs - injection lidocaine and ketamine infusions on the depth of anaesthesia during balanced anaesthesia, recovery profiles of the patients after surgery and anaesthesia and postoperative analgesia. So, we were planned to compare the effects of the injection lidocaine and ketamine infusions on the depth of anaesthesia during balanced anaesthesia BIS Scores, recovery profiles of the patients after anaesthesia and postoperative analgesia and hemodynamic parameters in patients undergoing abdominal surgeries under general anaesthesia in the form of a double blinded randomized controlled trial.

METHODOLOGY:

A double blinded randomized control trial has been conducted at Surgery Department in collaboration of Anaesthesiology department of Agartala Government Medical College over a period of one year from 2020- 2021 among the patient of both sexes with normal BMI of age between 18-60 years who underwent elective abdominal surgeries excluding mental insufficiency, head trauma, neurological disorders and heart disease individuals. The sample size calculated was 20 each intervention group considering of margin of error of 2% with total sample size 60.[9] Participants were recruited in the study upon informed consent. Block randomization with block size 6 was done. The interventions and control group were allocated in 1:1:1. Allocation concealment method was done in sequentially numbered opaque sealed envelope. It was a double blinded trial. After obtaining approval of the institutional ethical committee and informed consent, all randomized patients were given injection lidocaine loading (1.5mg/kg) over 10 mins and maintenance infusion (1.5mg/kg/hr) for Group L and Group K- were given injection ketamine loading (0.5mg/kg) and maintenance infusion. (0.5 mg/kg/hr) and Group C- were given injection normal saline as loading and maintenance solution. None of the investigators involved in patient management or data collection were aware of the group assignment. The data were collected and recorded in the case record format. For statistical analysis data were entered into a Microsoft excel spreadsheet and then analysed by SPSS 21.0. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two sample t-tests for a difference in mean involved independent samples or unpaired samples. Unpaired proportions were compared by Chi-square test or Fischer's exact test as appropriate. A p value ≤ 0.05 was considered statistically significant. Ethical approval was taken from institutional ethics committee, AGMC. The trial was registered in CTRI registration was done online after getting ethical committee approval. The patient's personal information's were kept confidential.

RESULTS:

20 in each intervention group enrolled and there is no lost to follow up. The mean age of the participants was 42.35 ± 7.22 years ranges from 30 to 54 years of age. The comparison of mean age of the participants among the study groups showed that group C have higher age (46.30 years) followed by group L (44.85 years) and group K (39.90 years) and the distribution is comparable with a p value of 0.06. Majority participants are female however, it is comparable in the group (p value 0.54). Bispectrality Index score shows lower range with lignocaine intervention (78.80±3.122) at 40-60 mg of dose compare to ketamine

and normal saline (90.65 ± 2.11 and 101.45 ± 3.2252 respectively) and these findings are found to be statistically significant with a p value of 0.001(table 1). The time of stoppage of study drug to extubation is more in group L (20.25 ± 2.198) than group K (19.70 ± 2.849) and group C (19.10 ± 1.858) and was found to be statistically insignificant with a p value of 0.16. Association of additional requirements of propofol with drug was statistically significant (p value 0.04). In group L, 6 (23.1%) patients had additional propofol. In group K, 8 (30.8%) patients had additional propofol. In group C, 12 (46.1%) patients had additional propofol. Bispectral index score (BIS) was found to be inconsistent as the time passes (at 5 minutes p= 0.408, 10 minutes p value 0.112, 15 minutes p value 0.115, 20 minutes p value 0.003, 25 minutes p value 0.44, 30 minutes p= 0.201, 35 minutes p value 0.016, 40 minutes p= 0.201, 45 minutes p=0.003, 50 minutes p= 0.05, 55 minutes p=0.142 and at 60 minutes p= 0.408. Table 2 shows heart rate profile comparison among study groups with p value (table 2) where intervention with group L shown significant control in heart rate as time progress. Both systolic and diastolic blood pressure also shown significant and better control with intervention group of lidocaine compared to ketamine and placebo. There were significant changes of mean arterial pressure in between the study group and group L shows better control at different observation (table 3). The mean comparison of SpO2 in all study groups shows that there is no significance difference of mean SpO2 in study groups during all observations. The study shows that VAS score over 24 hours was comparatively lower in group L than group K and group C during the observations at 15 minutes, 30 minutes, 2 hours, 4 hours, 8 hours and 12 hours with P value of 0.01, 0.002, 0.004, 0.04, 0.03 and 0.023 respectively. Time of first injection of diclofenac was given lately (241.01 mins) in group L comparatively than group K (128.21 mins) and group C (60.76 mins) and these differences were found to be statistically significant (p value 0.000) (Fig 1).

Table 1: Bolus of Propofol to reach target BIS (Bispectral index score) of 40-60 (in mg)

Study Group	N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
				Lower Bound	Upper Bound	
Group L	20	78.80	3.122	77.34	80.26	0.001*
Group K	20	90.65	2.110	89.66	91.64	
Group C	20	101.45	3.252	99.93	102.97	
Total	60	90.30	9.746	87.78	92.82	

**Statistically Significant*

Table 2: Heart rate (HR) changes among the study groups (N=60)

Heart rate observation time	Study group (mean & SD)			P value
	Group C	Group L	Group K	
5 mins	93.30 ± 12.53	94.85 ± 8.13	99.40 ± 9.11	0.149
10 mins	101.30 ± 4.55	97.95 ± 8.29	107.05 ± 8.29	0.001*
15 mins	110.30 ± 1.49	95.85 ± 6.49	99.20 ± 0.83	0.000*
20 mins	106.80 ± 9.90	106.55 ± 4.77	95.30 ± 11.64	0.000*
25 mins	101.30 ± 4.55	95.85 ± 6.49	99.20 ± 0.83	0.001*
30 mins	112.85 ± 3.57	96.45 ± 6.95	101.00 ± 6.88	0.000*
35 mins	106.80 ± 9.90	97.95 ± 8.29	95.30 ± 11.64	0.023*
40 mins	105.35 ± 2.30	93.25 ± 9.26	106.60 ± 8.46	0.000*
45 mins	106.80 ± 9.90	96.45 ± 6.95	99.20 ± 0.83	0.132
50 mins	109.05 ± 9.35	101.60 ± 3.21	101.20 ± 3.33	0.000*
55 mins	101.30 ± 4.55	95.85 ± 6.49	95.30 ± 11.64	0.001*
60 mins	108.06 ± 9.03	99.20 ± 0.83	99.60 ± 3.04	0.039*

**Statistically significant*

Table 3: Mean comparison of mean arterial pressure (MAP) in all study group (N=60)

MAP observation time	Study group (mean & SD)			P value
	Group C	Group L	Group K	
5 mins	103.95 ± 9.299	99.05 ± 8.918	100.30 ± 12.269	0.547
10 mins	112.85 ± 3.438	101.60 ± 9.970	112.10 ± 7.853	0.000*
15 mins	118.20 ± 8.167	101.70 ± 5.440	108.05 ± 15.133	0.000*
20 mins	119.25 ± 10.911	104.05 ± 12.959	116.15 ± 12.240	0.000*
25 mins	111.35 ± 4.146	112.10 ± 7.853	101.70 ± 5.440	0.001*
30 mins	121.50 ± 2.965	105.60 ± 9.230	112.10 ± 12.855	0.000*
35 mins	112.10 ± 7.853	118.20 ± 8.167	111.35 ± 4.146	0.000*
40 mins	119.20 ± 9.356	106.45 ± 9.282	106.95 ± 7.640	0.000*
45 mins	101.70 ± 5.440	111.35 ± 4.146	118.20 ± 8.167	0.000*
50 mins	117.20 ± 3.694	108.75 ± 1.333	111.35 ± 4.146	0.000*
55 mins	112.10 ± 7.853	118.20 ± 8.167	101.70 ± 5.440	0.001*
60 mins	111.35 ± 4.146	109.20 ± 8.621	116.00 ± 0.000	0.053

**Statistically significant*

The study finding also shows that Group L required only 2 doses of inj. diclofenac in the first 24 hours but other study groups received more than two doses of diclofenac injection. There was no nausea/vomiting was seen in all the groups. RAMSAY score was comparatively similar in all study groups (group L – 3, group K – 3 and group C- 2.35) with p value of 0.503. PADSS score was slightly higher in group L (301.12) compare to other study group (group K – 264.78 and group C-231.71 respectively) however, it is not found to be statistically difference (p value 0. 78).

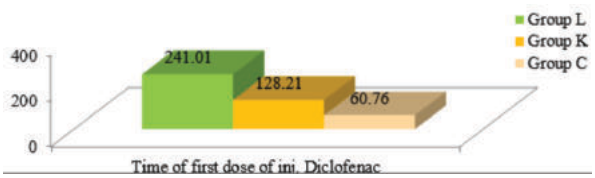

Fig 1: Time of first dose of diclofenac injection (minutes) in postoperative period

Table 4: Mean comparison of Quality of Recovery (QoR) Score in the study groups (N=60)

QoR domain	Group L -20 (Mean ± SD)	Group K -20 (Mean ± SD)	Group C-20 (Mean ± SD)	P value
Emotional State	44.30 ± 0.66	44.52 ± 0.46	44.75±0.52	0.2
Physical Comfort	59.56±1.36	58.32±0.60	58.76±0.50	0.01*
Psychological Support	35.72±0.57	34.70±0.01	34.00±0.00	0.7
Physical independence	24.73±0.68	24.66±0.58	24.95±0.22	0.1
Pain	34.950±0.31	34.55±0.60	33.25±0.52	0.02*
Combined QoR score	199.21± 3.58	196.75±2.25	194.69±1.58	0.01*

**Statistically significant*

The study result also shows that the Quality of recovery score in all the study groups showed that group L has better pain control and physical comfort with a p value of 0.02 and 0.01 respectively than group K and group C which was found to be statistically significant (table 4).

DISCUSSION:

In our study, it showed that gender distribution and age were comparable in between the study groups (p value 0.54 and 0.06), it means was almost equally distributed in all the groups. The body weight comparison between the groups were comparable. This study was similar to the study conducted by Imani F et al[10] and Tauzin-Fin P et al[11] on effects of ketamine and lidocaine Infusion on acute pain after

elective open abdominal surgery, a randomized, double-blinded study (2022) and found there was no statistically significant between age, sex and weight. Similar study was conducted by García-Navia JT et al[12] and found that there was no significant relation in demographic profiles of the patients in between the study groups. G.A. Hans et al[13] found that lidocaine decreased propofol requirements (P<0.05) only during surgery. In the absence of surgical stimulation, lidocaine did not affect BIS nor haemodynamic variables, whereas it reduced BIS increase (P=0.036) and haemodynamic response (P=0.006) secondary to surgery. In our study also shows similar findings. Weinbroum AA[14], Sarton E et al[15], Jagtiani A[16] and Hika A et al[6] showed there was statistically significant in HR and MAP after intubation with a p value <0.05 and also statistically significant in HR and MAP at immediate recovery at 3rd and 6th hour postoperative period with p value <0.05 which is incorporated with the present study. But as per Bhiwal AK et al[17] shown that there was no statistically significant in HR and MAP in ketamine and control groups. Our study results showed that group L and group K has better control haemodynamically except SpO2 in as it showed that there was no significant difference of mean SpO2 in the study groups during all the observations. It is similar to the previous literatures.[18,19,20] Kaur S et al[21] and Imani F et al[10] showed that evaluation of Visual analogue score (VAS) decreased significantly after 15 minutes till 12 hours after surgery in the patients of the LK (lidocaine and ketamine) group in comparison with the patients of the P (placebo) group (p<0.05). Some patients in both groups required additional analgesics (diclofenac suppositories). The sum of diclofenac suppository consumption during the first postoperative 24 hours was decreased significantly in the patients of the group L in comparison with the patients of the group K (p<0.001).[17,18,20] Ruchi Kumari, et al[8] also demonstrated similar findings. Jendoubi A et al[22] also found that both ketamine and lidocaine significantly reduced mean VAS pain scores versus placebo (P < 0.05) at rest and during cough or movement for up to 48 h postoperatively. The VAS pain scores were significantly lower in the LG compared with the KG in the first 12h postoperatively (P < 0.05). Ebied A et al[23] and Jendoubi A et al[22] had a better quality of recovery as assessed by the QoR score which is similar to this study finding.

In spite of every sincere effort my study has lacunae. The sample size was small. Only 60 cases were not sufficient for this study and single centred study. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.

CONCLUSION

The study concluded that perioperative lidocaine infusion is better than ketamine infusion in providing postoperative analgesia with minimal haemodynamic changes. Postoperative recovery profile is better with lidocaine infusion than ketamine infusion with no explicit recall in both the groups. Nevertheless, further studies are needed to determine the best perioperative lidocaine or ketamine regimen for postoperative pain control and prevention of controlling the confounders.

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