

Effectiveness of Intra-operative Intravenous Lidocaine Infusion as Part of Postoperative Analgesia for Patients Undergoing Abdominal Surgery under General Anesthesia in Addis Ababa Hospitals, Ethiopia 2018: Observational Cohort study

Assefa Hika^{1*}, Bacha Aberra¹, Mikael Azanaw², Wesenyeleh Admasu³, Degenah Bahrey⁴

¹Department of Anesthesiology, Aksum University, Aksum, Ethiopia; ²Department of Anesthesia, Empress Zewoditu Memorial Hospital, Addis Ababa, Ethiopia; ³Department of Anesthesia, Addis Ababa University, Addis Ababa, Ethiopia; ⁴Department of Adult Health Nursing, Aksum University, Aksum, Ethiopia

ABSTRACT

Introduction: Postoperative pain after abdominal surgery is excruciating, due to the damage of muscles and tissues. The importance of pain relief is well-recognized but it is most often seen that pain control is inadequate. Results of previous study shows the opioid consumption is 70% after abdominal surgery. An increasing amount of evidence suggests that intra-operative intravenous lidocaine infusion can influence pain severity, postoperative analgesic requirement and decrease opioid side effects.

Objective: The aim of this study was to assess analgesic effectiveness of intra-operative intravenous lidocaine infusion as part of postoperative analgesia for patients undergoing abdominal surgery under general anesthesia in Addis Ababa Hospitals.

Methods: Institutional based prospective cohort study conducted at Addis Ababa Hospitals among sixty eight elective abdominal surgery patients who were grouped into exposed and controlled group based on lidocaine (1mg/kg/hr) given or not. Systematic random sampling was employed. Mann Whitney U test was used to compare median pain score, time to first analgesia request in minutes and total analgesia consumption between groups. Homogeneity of categorical independent variable between two exposure groups was analyzed using Chi Square or Fisher's exact test. Box and whisker plot were used to show a median pain score differences between groups and p value <0.05 considered as statistical significance with a power of 80%.

Result: Demographic characteristics were comparable between the groups, $p > 0.05$. Twenty four hour median VAS score (0-10 cm) at immediate recovery, 3rd, 6th, 12th and 24th hour showing lower median pain score, $p < 0.05$. The median time to first analgesia request in minutes were longer (180 minutes) in exposed group compared to 45 minutes in non-exposed group ($p = < 0.0001$). The median tramadol consumption within 24 hour is 50 mg in exposed group compared to 100 mg in non-exposed group ($p < 0.0001$).

Conclusions: Intra-operative lidocaine infusion decreases postoperative pain score, total analgesia consumption and prolongs time to first analgesia request for abdominal surgery done under general anesthesia.

Keywords: Lidocaine infusion; Pain; Abdominal surgery; Visual analogue score (VAS)

Correspondence to: Assefa Hika, Department of Anesthesiology, College of Health Science, Aksum University, Aksum, Ethiopia, Tel: +913785495; E-mail: bcassefa@gmail.com

Received: June 2, 2020 ; **Accepted:** July 1, 2020 ; **Published:** July 8, 2020

Citation: Hika A, Aberra B, Azanaw M, Admasu W, Bahrey D (2020) Effectiveness of Intra-operative Intravenous Lidocaine Infusion as Part of Postoperative Analgesia for Patients Undergoing Abdominal Surgery under General Anesthesia in Addis Ababa Hospitals, Ethiopia 2018: Observational Cohort study. J Anesth Clin Res. 11: 954. DOI: 10.35248/2155-6148.20.11.954.

Copyright: © 2020 Hika A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

List of abbreviations

ASA: American Society of Anesthesiologist, BP: Blood Pressure, GA: General Anesthesia, HR: Heart Rate, IASP: International Association for Study of Pain, IVLI: Intra Venous Lidocaine Infusion, MAP: Mean Arterial Pressure, Mg/kg/hr: milligram per kilogram per hour, MmHg: millimeter of mercury, NSAIDS: Non-Steroidal Anti-Inflammatory Drugs, OR: Operation Room, PACU: Post Anesthesia Care Unite, PCA: Patient Controlled Analgesia, PONV: Post-Operative Nausea and Vomiting, VAS: Visual Analogue Scale

INTRODUCTION

Abdominal surgery involves a surgical operation on organs inside the abdomen. This may include surgery on the stomach, gallbladder, small intestine, or large intestine (colon), liver, pancreas, spleen, esophagus, and appendix [1]. General or regional anesthesia can be appropriate for patients undergoing abdominal surgery. In common practice, balanced anesthesia with inhalational anesthetics, opioids and neuromuscular blockers are used in general anesthesia for abdominal surgical procedures. Abdominal wall incision is the major origin of pain experienced by patients after abdominal surgery. Through systematically administered opiates and central neuraxial techniques cause considerable adverse effect, they remain the mainstay analgesic after abdominal surgery. The mean postoperative pain score of 6.5 cm were reported on 10 cm Visual Analog Scale (VAS). It has been also reported that the morphine consumptions in the first postoperative day is 70%. The proportions of patient with pain score greater than 3 cm is 60% on VAS score [2,3].

Many strategies have been implemented to reduce postoperative pain following abdominal surgery, including steroidal anti-inflammatory drugs, administration of opioid, and neuroaxial anesthesia. However, most of the time they did not show consistent efficacy. Thus, multimodal analgesia regime was recommended for pain management after abdominal surgery [18]. Besides of decreasing cost and side effect of opioids, use of lidocaine infusion also support the principle of multimodal analgesia where a variety of analgesic medication and techniques that target different mechanisms of action in the peripheral or central nervous system (which might also be combined with non-pharmacological interventions) might have additive or synergistic effects or alternative analgesia and more effective pain relief compared with single-modality interventions [19-21].

Study of effective modality for postoperative pain management has remained a subject of ongoing clinical researches due to its uniqueness and associated complex physiological consequences with somatic, autonomic and behavioral manifestations. The importance of pain relief is well-recognized but it is most often seen that pain control is inadequate. The role of a well-planned pain management strategy in the immediate postoperative period is crucial to decrease postoperative cognitive impairment, enhanced quality of life, reduced risk of chronic or persistent post-surgical pain and morbidity after abdominal surgery, aided by the availability of multitude of drugs, dosages and routes of administration [4,6].

Intravenous (IV) infusion of lidocaine is one of the methods used by anesthesiology specialists for induction of analgesia. Lidocaine is a relatively safe drug in the amide group, which acts as an analgesic, anti-hyper-algesia and anti-inflammatory agent in low doses and is affective in relieving neuralgia, burn and procedural pains [7,8].

An increasing amount of evidence suggest that peri-operative intravenous lidocaine can influence pain severity, postoperative analgesic requirement, recovery of bowel function and the length of hospital stay, without any significant side effects than analgesics alone [5,9,10].

There are also different controversies among different authors worldwide on effect of lidocaine infusion on postoperative period. Even the pain management style also varies due to economic and technological difference to our study area. These controversies were one of the reasons which call for the study [4,20].

MATERIALS & METHODS

Study setting

The study was conducted in Addis Ababa hospitals, Addis Ababa, is capital city of Ethiopia. Today the hospitals are administered by Addis Ababa Health Bureau. According to the nine month report of policy and plan directorate of the hospitals compiled on July 2017, the hospitals provide service to an estimated 15,700 people annually in different departments who are referred from different part of the city and all over the country. Out of this, 500 patients are expected to undergo abdominal surgeries. The general surgery department of the hospitals has 33 surgical beds, 5 senior surgeons and 10 surgery residents. It has five major operation rooms and two PACU.

Institution based prospective observational cohort study was employed from February 1 to April 30, 2018, after ethical approval (No-93/2010, Dec 11, 2017) was obtained from the Addis Ababa University Ethical committee.

patients of age greater than 18 years and ASA class I and II, that undergone elective abdominal surgery under general anesthesia was included in the study. Patient who have allergy for local anesthetics and has history of chronic opioid use, Induction with ketamine, Liver dysfunction, and renal insufficiency has been excluded from study.

In this study, the dependent variables were Pain severity by VAS score (0-10cm), time to first analgesic request in minutes and total analgesia consumption in milligram in the first 24 hours. The independent variables were socio-demographic and operative data (Age, sex, Body Mass Index (BMI), Preoperative surgical diagnosis, Induction agent, Maintenance agent, Peri-operative analgesia, Duration of surgery in minute, Duration of anesthesia in minutes.

Sample size and sampling techniques determination

Two independent sample size formula based on the mean difference of VAS score, time to first analgesia request and total analgesia request among two groups were used to calculate

sample size for each group. Having no previous study done in the study area, result adopted from literature has been used to calculate sample size based on the three outcome variable and the largest sample size were used for recruiting study subjects.

The required sample size to show with 95% likelihood that the mean VAS score within 24 hour is not equal between two groups was calculated as:

Where n = the sample size in each of the groups

X 1 = Sample mean in control group

X 2 = Sample mean in treatment group

$$n = \frac{(S1^2 + S2^2) (\alpha + \beta)^2}{(X1 - X2)^2}$$

X 1-X 2=the difference the investigator wishes to detect

S21=Sample variance in control group

S22=Sample variance in treatment group

α =conventional multiplier for alpha =0.05, which is 1.96

β =conventional multiplier for power = 0.80, which is 0.842

From the literature the mean VAS score, $\mu_1=3.5$ in control group, $\mu_2=1.6$ in treatment group and $\sigma_1=3.1$, $\sigma_2=2.4$ [15]. Substituting for this variables yields

$$n = \frac{(3.1)^2 + (2.4)^2 \times (1.96+0.842)^2}{(3.5-1.6)^2}$$

$n=33=n_1=n_2$, using 1:1 ratio between groups a total of 66 patients were required.

By adding 10% for non-respondent rate in each group, 72 patients were included in the study. But 4 patients were excluded from the study due to incomplete data. Therefore, 68 patients were analyzed in the study with a response rate of 94.4%.

Sampling Technique

Systematic random sampling was used to select study participants. The daily operation schedule list was used as a sampling frame. The situational analysis showed that 10 patients who fulfill our inclusion criteria were operated in Addis Ababa Hospital per week that got from surgery logbook record; according to this data we were had 120 patients in our study period from whom we collected data from only 72 patients.

So, sampling interval (k) was calculated as $K=N/n=120/72$, approximately 2, where N=total study population, n=total sample size. The first participant was selected randomly using lottery method. Then, every two patients were included in this study from the daily operation schedule list until the required sample size was met and grouped based on whether they

received lidocaine infusion (exposed group) or not (controlled group).

Intra-operative procedure

After preoperative preparation, patients were shifted to the operation room, standard monitoring applied as routine. Baseline vitals were recorded and I.V. fluids were administered

Anesthesia management for abdominal surgery in study hospital is carried out by M.Sc. B.Sc. and diploma anesthesia professionals. M.Sc. anesthesia professionals including M.Sc. anesthesia students and some B.Sc. anesthetists provide lidocaine infusion using a bolus dose of 1.5mg/kg of lidocaine before induction of anesthesia. Then immediately after induction they continued IV infusion of 1mg/kg per hour of lidocaine mixed with 500ml of 0.9% normal saline using aonmed infuser for 60 minutes intra-operatively. Those diploma and some anesthesia professionals did not provide lidocaine infusion as supplementary to general anesthesia (GA).

In the postoperative time patients transferred to recovery room and transferred to ward when they recover from anesthesia. In ward patient were usually observed by ward nurses and pain is usually managed by tramadol and diclofenac based on patient complain and sometimes on physician order.

At PACU patients were asked to mark their pain level based on 0-10cm VAS score as soon as patient fully respond to verbal command and recovered from full cognitive ability. VAS score and other variables were documented at 3rd hour, 6th hour, 12th hour and 24th hour at wards after end of surgery. A time in minutes from end of surgery to first analgesia request were documented together with total analgesia consumed in the first 24 hours. In addition, incidence of postoperative nausea and vomiting documented when it was reported within 24 hours.

Data collection technique and instrument

Data were collected using a pretested observational checklist. Data collectors were one bachelor degree holder anesthetist and two bachelor degree holders nurse and they supervised by one master degree holder anesthetist.

Questionnaires were prepared in both in English and Amharic languages and it was divided in to three parts, the first one was filled in the preoperative and intra-operative time and collected by one trained BSc anesthetist and the second one was PACU record going to be recorded by PACU nurse and the third one was filled in the ward which was filled by trained ward nurse.

Data quality assurance

Pretest was done for one week at Addis Ababa Hospitals with 5% of the total sample size (two patients in each group) which were not included in the actual study. Collected data were checked for completeness, accuracy and clarity. Incomplete data were not entered a data base prepared on Epi-info. Data clean up and cross-checking was done before analysis on SPSS. Regular supervision was done during data collection by principal investigator and M.Sc. anesthesia students and data was stored in safe and secured place.

Data processing and analysis

The data were reviewed from completed structured data retrieval form to ensure completeness and quality of data. After data quality was assured, forms were collected and assigned consecutive number (code) for ease of data entry. The Data was entered using the Epi-Info version 7.0 and clean-up has been made to check accuracy, consistency and errors identified were corrected and finally transported to SPSS V 20 for analysis.

Shapiro Wilk test with p value <0.05 for non-normally distributed data and histogram with bell-shaped were used to test for normal distributions of data while homogeneity of variance were assessed using Levene’s test for equality of variance. Numeric data were described in terms of mean ± SD for symmetric data like age, BMI, heart rate(HR) and median (Inter-quartile range) for asymmetric numeric data like 24 hour VAS score and total analgesia consumption. Comparison of numerical variables between study groups were done using unpaired student t-test and Manny Whitney U test based on symmetric and asymmetric data respectively.

Frequency and percentage were used to describe categorical variable and statistical association between groups were tested using Chi-square for data like sex, surgical procedures and surgeons experience or Fisher’s exact test for data like ASA status. The findings of the study are presented in tables and figures. A p-value <0.05 with power of 80% considered statistically significant.

Operational definitions

Postoperative pain: A patient complaining pain and any pain score other than zero within 24 hours.

Post-operative nausea and vomiting: When a patients experience at least one episode of either nausea or vomiting within 24 hours.

Intra-operative hemodynamic changes: Change in heart rate (HR) and mean arterial pressure (MAP) during surgery.

Duration of surgery: Time in minutes from skin incision to end of surgery.

Duration of anesthesia: A time in minutes it takes from pre oxygenation to a time a patient get response to verbal command.

Time to first analgesia request: A time in minutes from the end of surgery to a first time analgesia were given.

Total analgesia consumption: Total dose of anti-pain medication given in mg within the first 24 hour after end of surgery.

Extubation time: is a time in minutes estimated from closure of halothane vaporizer to extubation of endotracheal tube.

Vital sign before induction: Is a base line HR and MAP of a patient before giving any anesthetic drug.

RESULTS

Demographic and Peri-operative Characteristics of study participants

A total of Sixty eight patients were included in our study. About 59 (86.8%) of study patients were ASA I and 9 (13.2 %) were ASA II. The mean BMI (kg/m²) in exposed group is 22.78 ± 1.69 kg/m² and non-exposed group is 22.68 ± 1.59kg/m² which is comparable in both groups, p=0.802. The mean age in exposure group and control group is comparable with 40.7 ± 7.6 years) and 44.4 ± 8.8 years, P=0.068.

Majority of patients underwent laparotomy and cholecystectomy surgical procedures in both groups with a proportion of 24(35.3%) and 22(32.3%) respectively. The remaining surgical procedures include resection anastomosis 11(16.2%), colostomy closure 8(11.8%) and ileostomy closure 3(4.4%) in both groups.

There was no statistical difference between the two groups in other peri-operative characteristics, p>0.05 as showed in (Table 1).

Variables	Exposed (lidocaine)	Non-exposed
	Group (n=34)	Group (n=34)
Age (years) (mean ± SD)	40.7 ± 7.6	44.4 ± 8.8
BMI(kg/m ²) (mean ± SD)	22.78 ± 1.69	22.68 ± 1.59
Sex	Male (n, %)	21 (30.9%)
	Females (n, %)	13 (19.1%)
ASA Status	ASA I (n, %)	28 (41.2%)
	ASA II (n, %)	6 (8.8%)
Surgical procedures	Cholecystectomy	10 (14.7%)
	Laparotomy	13 (19.1%)

	Resection anastomosis	6 (8.8%)	5 (7.4%)
	Colostomy closure	4 (5.9%)	4 (5.9%)
	Ileostomy closure	1 (1.5%)	2 (2.9%)
Induction agent	Thiopental	19 (27.9%)	12 (17.6%)
	Propofol	15 (22.1%)	22 (32.4%)
Surgeon experience	Resident (n, %)	20 (29.4%)	18 (26.5%)
	Senior (n, %)	14 (20.6%)	16 (23.5%)
Estimated intraoperative blood loss (ml) #		130 (120-170)	130 (110-150)
Duration of surgery (minutes)#		78 (74-80)	80 (75-84)
Duration of anesthesia (minutes)#		87.5 (85-90)	90 (85-90)
Extubation time (minutes) #		4 (3-5)	5(3-5)

Twenty four hour VAS score

The median VAS scores in lidocaine group remained significantly less than that in controlled group (p<0.05) (Table2). The median VAS score were lower in the exposed group at recovery room, 3rd, 6th, 12th, and 24th hour. Using Many Whitney test a significant statistical difference were observed at all time between exposed and non-exposed groups with p-value <0.05 (as shown in figure 1).

Comparison of Time to First Analgesia Request and Total Analgesia Consumption between Groups

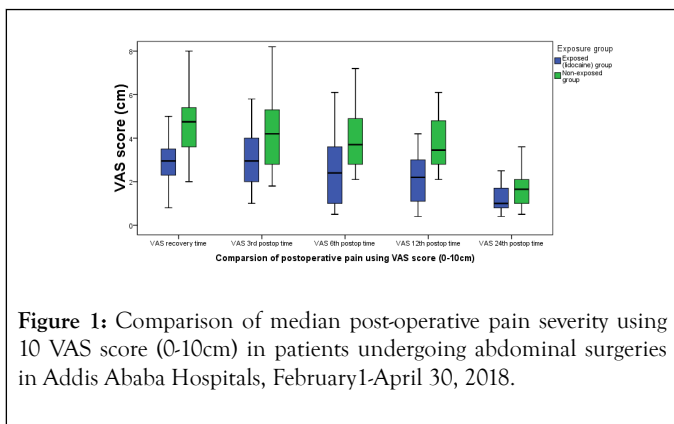
The median time in minutes were longer 180 minutes in exposed group compared to 45 minutes non-exposed group, p<0.0001. There were also statistically significant differences with regard to median total tramadol consumption within 24 hours. There were no statistical differences between two groups in total diclofenac consumption (Table 3).

Table2: Comparison of postoperative pain severity using median(IQR) VAS score (0-10cm) at recovery room, 3rd, 6th, 12th and 24th postoperative time in patients undergoing abdominal surgeries in Addis Ababa Hospitals, February 1-April 30, 2018. Using Mann-Whitney U test (median and IQR).

Variables expressed as median (IQR) in (cm)	Exposed(Lidocaine) group (n=34)	Non-exposed group (n=34)	p-value
Recovery room VAS score	2.9 (2.3-3.5)	4.7 (3.6-5.4)	<0.0001
3 rd post-operative time VAS score	3.0 (2.0-4.0)	4.2 (2.8-5.3)	0.011
6 th post-operative time VAS score	2.4 (1.0-3.6)	3.7 (2.8-4.9)	0.001
12 th post-operative time VAS score	2.2 (1.1-3.0)	3.3 (2.8-4.0)	<0.0001
24 th post-operative time VAS score	1.0 (0.8-1.7)	1.6 (1.0-2.1)	0.02

Table3: Comparison of median time to first analgesia request in minutes and median total analgesia consumption between two groups in the first 24 hour.

	Exposed (Lidocaine) group (n=34)	Non-exposed group (n=34)	p-value
Time to first analgesia request in minutes	180 (60-240)	45 (45-60)	<0.0001*
Total analgesia consumption within 24 hour	Tramadol (IV)	100 (100-150)	<0.0001*
	Diclofenac (IM)	75 (75-75)	0.18



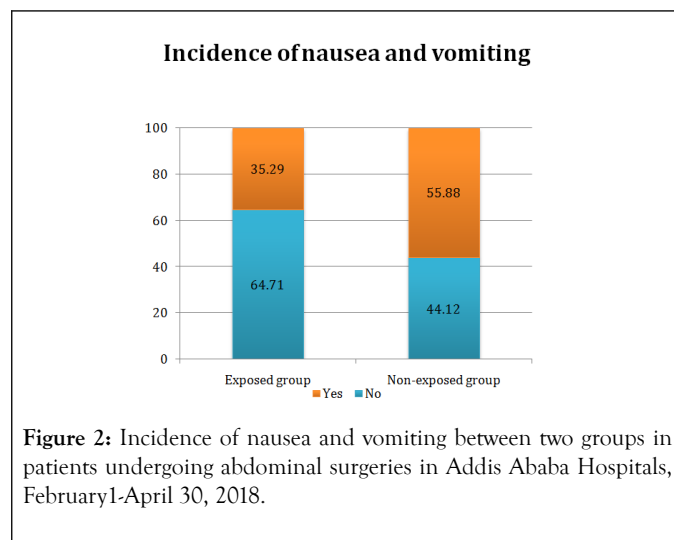
Incidence of Nausea and Vomiting between exposed and non-exposed group

The incidence of nausea and vomiting over 24 hours is 45.6%. The proportions of patients with nausea and vomiting in exposed group (lidocaine) is (35.3%) and (55.9%) in non-exposed group with (X² =2.134) and a p value of 0.144 (as shown in a figure 2).

Comparison of HR and MAP before induction, after intubation and 24 hour postoperative period between the two groups

There is no statistical significance result shown between the two groups in HR and MAP before induction of anesthesia, p>0.05

but there is a statistical significance result shown between the two groups in HR and MAP after intubation with p value <0.05.



Also Statistically significant result was found in HR and MAP between two groups at immediate recovery room, 3rd and 6th hour's postoperative time, p<0.05 but there is no statistically significance regarding HR and MAP at 12th and 24th postoperative, p>0.05 as shown below in Table 4.

	Exposed (lidocaine) group (n=34)	Non-exposed group (n=34)	p-value
Vital sign before induction of anesthesia			
HR (mean ± SD)	80 ± 9	82 ± 9	0.268
MAP (median and IQR)	92 (89-97)	93 (89-100)	0.299
Vital sign after intubation			
HR (median and IQR)	95 (92-100)	101 (96-109.8)	0.002*
MAP (mean ± SD)	95 ± 4	104 ± 6	<0.0001*
Immediate recovery room (PACU) vital sign			
HR (median and IQR)	68(67-73)	79(78-89)	<0.0001*
MAP (median and IQR)	87(82-90)	90(87-95)	0.008*
Vital sign at 3rd hour			
HR (median and IQR)	71(67-76)	81(76-87)	<0.0001*
MAP (median and IQR)	84(78-88)	89(82-93)	0.003*
Vital sign at 6th hour			

HR (median and IQR)	77(72-88)	87(79-96)	0.013*
MAP (median and IQR)	81(78-89)	88(86-93)	0.019*
Vital sign at 12th hour			
HR (median and IQR)	80(74-86)	85(78-91)	0.186
MAP (median and IQR)	84(78-88)	89(79-90)	0.055
Vital sign at 24th hour			
HR (median and IQR)	78(72-84)	79(75-83)	0.551
MAP (median and IQR)	87(79-89)	88(85-90)	0.127

HR=Heart Rate, MAP=Mean Arterial Pressure IQR=Inter-quartile range,*=statistically significant

DISCUSSION

The present study showed that the median pain score at rest were lower 2.9(2.3-3.5) in exposed group compared to 4.5 (3.6-5.4) in non-exposed group with p value of <0.0001 at immediate recovery room. The median VAS score at 3rd post-operative hour in exposed group is lower 3.0 (2.0-4.0) compared to 4.2 (2.8-5.3) in non-exposed group p value of 0.011. The median postoperative pain score were also lower at 6th, 12th and 24th post-operative time with statistically significant difference of 0.001, <0.0001 and 0.020 respectively.

A meta-analysis in China aimed to assess the efficacy and safety of intravenous infusion of lidocaine for pain management after cholecystectomy concluded that there were significant difference between groups in terms of VAS scores at 24 hours, p<0.05 and significant difference were found regarding opioid consumption at 24 hours, p=0.009 [18].

The result of our study is in line with study done in Iran showing the lower pain score in treatment group compared to the control group. This double blinded randomized controlled study demonstrate that the mean \pm SD pain score in treatment group is 3.72 \pm 0.56 and 5.50 \pm 0.53 cm in control with placebo group respectively, p=0.0001. The likely explanation for the similarity between two studies is the infusion were given starting with loading dose of lidocaine 1.5mg/kg before induction of anesthesia and continue with infusion of 1mg/kg immediately after induction of anesthesia in both studies except the later one study have used intra-operative fentanyl (strong opioid) as additional analgesia and VAS score at 24th hour was not significant with p=0.64 due to difference in post-operative analgesia used [9].

Our study supports the findings of the study done in Nepal with the mean pain VAS scores in lidocaine group remained significantly less than that in control group with mean VAS score at 3rd hour is 2.5 \pm 1.4 and 3.6 \pm 1.7 respectively (p<0.001) [14].The analgesic efficacy of lidocaine is due to a selective depression of pain transmission in the spinal cord and a reduction in tonic neural discharge of active peripheral nerve fibers [2,22].

In contrary to our study a randomized controlled trail done in Switzerland to analyze the effect of peri-operative IV lidocaine in laparoscopic renal surgery postoperative pain scores showed there were no significant differences between groups in pain scores over time at rest with analgesic efficacy of lidocaine intra-operative infusion of 1mg/kg/hr. The mean NRS score at 6th hour is 4 \pm 2 in lidocaine group compared to 5 \pm 1 in control group with 0-10 NRS scale (p=0.71). The possible explanation for this contradictory result is the use of fixed postoperative pain treatment (co-analgesic agents) like administering metamizole and paracetamol (acetaminophen) every 6 hours postoperatively and difference in study design [10].

Our study showed significantly less total postoperative analgesic (tramadol) requirement in lidocaine group than in control group. The median (IQR) tramadol in mg where 50(50-100) mg in exposed group compared to 100(100-150) mg in non-exposed group p<0.0001. We lack similar finding for comparison with the same drug tramadol (weak opioid) since most studies are using strong opioids (morphine) as postoperative pain management protocol and controlling of analgesic agent achieved between groups. The mechanisms of analgesia of this local anesthetic on surgical trauma include neuronal transmission blockage at the place of injury, reducing neurogenic response and systemic anti-inflammatory intrinsic activity. Lidocaine's analgesic property can persist even after the decreasing of its plasmatic levels, which corroborates the nervous conduction blockage theory [5].

Though different drugs were used, study done in America reveals total postoperative morphine consumption in lidocaine group is lower than that of control group with mean 17 \pm 1.5 mg compared to 25 \pm 2.7 mg respectively with p <0.0001. Though our study use the weakest opioid, the opioid conversion factor of 1mg tramadol compared or equal to 0.1mg of morphine which estimates 100mg tramadol to 10mg morphine which is comparable and equivalent analgesic effect [18]. The scientific explanation for this similar result is when systemic lidocaine is administered during operation it will prevent the induction of central hyperalgesia leading to morphine sparing effects by direct inhibition to N-methyl-D-Aspartate (NMDA) receptor, while peripherally decreasing spontaneous neuronal discharge

from A delta and C fibers thus decreasing transmission of nociceptive pain) [2,8,21].

In contrary to our finding controlled study done in Switzerland, didn't demonstrate analgesic efficacy of lidocaine infusion in terms of total analgesia consumption. The result shows no statistically significant difference between two groups regarding total cumulative postoperative morphine consumption during the first 24 hour (7 ± 9 mg) vs. 11 ± 12 mg) in lidocaine infusion and control group respectively with $p=0.23$ [10]. The likely explanation for this contradictory finding is additional intraoperative use of 70% nitrous oxide combination with oxygen as maintenance of anesthesia difference which have additional analgesic effect and variability in caregiver's response to pain request because the study might be used patient controlled analgesia (PCA) (objective) for more accurate evaluations of pain than VAS score (subjective). Availability of resources or medication used to manage pain up on request also a big reason to this difference observed in the study set up.

A double-blinded study by Saadawy and collaborators in 120 patients submitted to laparoscopic cholecystectomy using the lidocaine infusion for post-operative pain management showed that, there was lower need of morphine use at the second postoperative hour. The lidocaine group had lower scores of abdominal pain at rest with 2, 6 and 12 hour postoperative. The scientific reason for result similarity between the studies is that lidocaine and its metabolites interacts with peripheral and central voltage-gated sodium channel on intracellular face of membrane blocking the start and conduction of neural impulse potential and morphine sparing effect [5,11].

We also observed the median (IQR) of total diclofenac consumption within 24 hours which is not statistically significant between lidocaine and saline groups (75mg (0-75mg) vs. 75mg (75-75mg) respectively ($p=0.180$). We lack similar finding for comparison since most studies are using opioids as postoperative pain management protocol and controlling of analgesic agent achieved between groups. Thus, lack of settled standard postoperative pain management protocol in the study hospital was among the possible factor for the similarity of diclofenac consumption between exposed and non-exposed group.

Our study demonstrate the median(IQR) time for the request of the first dose of analgesic was significantly longer in lidocaine group than in control group 180(60-240)minutes vs. 45 (45-60)minutes, $p<0.0001$. Our finding is comparable with study done in Nepal which shows mean time for the first analgesic request time was longer in treatment group compared to control group, 60.97 ± 18.05 minutes vs. 15.73 ± 7.46 minutes, respectively, ($p<0.001$) [14].

The persistence of analgesic effect of lidocaine even after the infusion was discontinued in our study indicates prevention of spinal or peripheral hypersensitivity or both to painful stimuli reflecting its effects on inhibition of spontaneous impulse generation arising from injured nerve fibers and from dorsal root ganglion neurons proximal to the injured nerve segments and suppression of primary afferent evoked polysynaptic reflexes in the spinal dorsal horn. These effects have been postulated to

be mediated by a variety of mechanisms, including sodium channel blockade, as well as inhibition of G protein-coupled receptors, N-methyl-D-aspartate receptor, reduces circulating inflammatory cytokines, and prevents secondary hyperalgesia and central sensitization [20].

Our finding shows the overall incidence of nausea and vomiting after elective abdominal surgery in the first 24 hours to be 45.6%. This proportion is higher in the control group with incidence of 55.9% compared to 35.3% in the treatment group. Though there is a proportion difference, there is no statistical difference between two groups with regard to decreasing the incidence of nausea and vomiting in the first 24 hours ($p=0.144$). This shows a proportion difference compared to study by Samimi *et al.* where the incidence of postoperative nausea and vomiting is 26%, $p=0.081$ [8]. The likely explanation for this incongruity is, Samimi *et al.* had used propofol as standard induction agent which is known for decreasing incidence of nausea and vomiting and also this might be because the total amount of fentanyl which can induce nausea and vomiting, had been significantly lower in lidocaine group in the study and different in type and depth of inhalational anesthetic agent is the other likely explanation.

There is a statistical significant difference between two groups in HR and MAP after intubation, $p<0.05$ but no significance difference between two groups in HR and MAP before induction of anesthesia, $p>0.05$. Attenuation of the sympathetic response (increase in HR and MAP) during laryngoscopy and endotracheal intubation was observed in the lidocaine group. The result of this study is in line with randomized controlled study done in Turkey showed that heart rate after intubation was significantly lower in lidocaine group compared with controlled group ($P<0.05$) [9]. The likely scientific explanation for this result is lidocaine affects impulse conduction from Sino-atrial (SA) node of the heart and decreases HR and systolic blood pressure.

CONCLUSIONS

It can be concluded that intra-operative infusion dose of lidocaine 1 mg/kg/hr decreases the intensity of postoperative pain, reduces the postoperative analgesics requirement, prolongs time to first analgesic request and as a part of multimodal approach for post-operative analgesia in patients underwent abdominal surgery.

LIMITATIONS

Difficult to measure the plasma concentration of lidocaine to understand its pharmacokinetics. In addition most of studies we have used for comparison of our result median (IQR) were with mean (SD) of literatures and most of them were randomized control trials (RCT).

DECLARATION

We, the undersigned, declare that this paper is our original work has never been presented in any University and we understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced.

ETHICAL APPROVAL

Ethical clearance and approval were obtained from the ethical review committee, Addis Ababa University College of health sciences. Permission to conduct was obtained from Addis Ababa Hospitals. The purpose of the study was explained to patient and the family of patients under the study and written informed consent was obtained from each patient. The patients' was informed that the care to be given was not be compromised in any way and confidentiality was assured. Name and other identifying information were not used in the study.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

ACKNOWLEDGMENTS

The authors acknowledge Addis Ababa University, the supervisors, data collectors, and study participants for their invaluable support.

REFERENCES

- Alagol A. Anesthetic management of abdominal surgery. *Abdominal Surgery*. 2012;14:55.
- McCarthy GC, Megalla SA, Habib AS. Impact of intravenous lidocaine infusion on postoperative analgesia and recovery from surgery. *Drugs*. 2010;70(9):1149-1163.
- Terkawi AS, Tsang S, Kazemi A, Morton S, Luo R, Sanders DT, Regali LA, Columbano H, Kurtzborn NY, Durieux ME. A clinical comparison of intravenous and epidural local anesthetic for major abdominal surgery. *Regional Anesthesia & Pain Medicine*. 2016;41(1):28-36.
- Weibel S, Jokinen J, Pace N, Schnabel A, Hollmann M, Hahnenkamp K, et al. Efficacy and safety of intravenous lidocaine for postoperative analgesia and recovery after surgery: a systematic review with trial sequential analysis. *British journal of anaesthesia*. 2016;116(6):770-783.
- Mendonça FT, Reis MC, Aguiar JA, Calvano LA. Systemic Lidocaine for Perioperative Analgesia: A. *JAICM*. 2015;1(1):7.
- Gupta A, Kaur K, Sharma S, Goyal S, Arora S, Murthy R. Clinical aspects of acute post-operative pain management & its assessment. *Journal of advanced pharmaceutical technology & research*. 2010;1(2):97.
- Forouzan A, Barzegari H, Motamed H, Khavanin A, Shiri H. Intravenous Lidocaine versus Morphine Sulfate in Pain Management for Extremity Fractures; a Clinical Trial. *Emergency*. 2017;5(1).
- Samimi S, Taheri A, Tanha FD. Comparison between intraperitoneal and intravenous lidocaine for postoperative analgesia after elective abdominal hysterectomy, a double-blind placebo controlled study. *Journal of family& reproductive health*. 2015;9(4):193.
- Zengin SU, Saracoglu A, Eti Z, Umuroglu T, Gogus FY. The effects of preoperative oral pregabalin and perioperative intravenous lidocaine infusion on postoperative morphine requirement in patients undergoing laparotomy. *Pain Research and Management*. 2015;20(4):179-182.
- Wuethrich PY, Romero J, Burkhard FC, Curatolo M. No benefit from perioperative intravenous lidocaine in laparoscopic renal surgery: a randomised, placebo-controlled study. *European Journal of Anaesthesiology (EJA)*. 2012;29(11):537-543.
- Meissner W, Coluzzi F, Fletcher D, Huygen F, Morlion B, Neugebauer E, et al. Improving the management of post-operative acute pain: priorities for change. *Current medical research and opinion*. 2015;31(11):2131-2143.
- Yarwood J, Berrill A. Nerve blocks of the anterior abdominal wall. *Continuing Education in Anaesthesia, Critical Care & Pain*. 2010;10(6):182-186.
- Mann C, Pouzeratte Y, Boccaro G, Peccoux C, Vergne C, Brunat G, et al. Comparison of intravenous or epidural patient-controlled analgesia in the elderly after major abdominal surgery. *Anesthesiology: The Journal of the American Society of Anesthesiologists*. 2000;92(2):433.
- Baral B, Bhattarai B, Rahman T, Singh S, Regmi R. Perioperative intravenous lidocaine infusion on postoperative pain relief in patients undergoing upper abdominal surgery. *Nepal med coll J*. 2010;12(4):215-220.
- Grady P, Clark N, Lenahan J, Oudekerk C, Hawkins R, Nezat G, et al. Effect of intraoperative intravenous lidocaine on postoperative pain and return of bowel function after laparoscopic abdominal gynecologic procedures. *AANA journal*. 2012;80(4).
- Eipe N, Gupta S, Penning J. Intravenous lidocaine for acute pain: an evidence-based clinical update. *Bja Education*. 2016;16(9):292-298.
- Woldehaimanot TE, Eshetie TC, Kerie MW. Postoperative pain management among surgically treated patients in an Ethiopian hospital. *PloS one*. 2014;9(7):e102835.
- Zhao J-B, Li Y-L, Wang Y-M, Teng J-L, Xia D-Y, Zhao J-S, et al. Intravenous lidocaine infusion for pain control after laparoscopic cholecystectomy: A meta-analysis of randomized controlled trials. *Medicine*. 2018;97(5).
- Kandil E, Melikman E, Adinoff B. Lidocaine infusion: a promising therapeutic approach for chronic pain. *Journal of anesthesia & clinical research*. 2017;8(1).
- Dunn LK, Durieux ME. Perioperative use of intravenous lidocaine. *Anesthesiology: The Journal of the American Society of Anesthesiologists*. 2017;126(4):729-737.
- Dewinter G, Van de Velde M, Fieuws S, D'Hoore A, Rex S. Transversus abdominis plane block versus perioperative intravenous lidocaine versus patient-controlled intravenous morphine for postoperative pain control after laparoscopic colorectal surgery: study protocol for a prospective, randomized, double-blind controlled clinical trial. *Trials*. 2014;15(1):476.
- Kranke P, Jokinen J, Pace NL, Schnabel A, Hollmann MW, Hahnenkamp K, et al. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery. *The Cochrane Library*. 2015.
- Choi SJ, Kim MH, Jeong HY, Lee JJ. Effect of intraoperative lidocaine on anesthetic consumption, and bowel function, pain intensity, analgesic consumption and hospital stay after breast surgery. *Korean journal of anesthesiology*. 2012;62(5):429-434.
- Mudiganti RKR, Magam RR, Rambabu T. Attenuation of haemodynamic changes during laryngoscopy and endotracheal intubation using IV lidocaine versus IV cloridine. *Indian Journal of Clinical Anaesthesia*. 2016;3(2):224-232.
- Vigneault L, Turgeon AF, Côté D, Lauzier F, Zarychanski R, Moore L, et al. Perioperative intravenous lidocaine infusion for postoperative pain control: a meta-analysis of randomized controlled trials. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*. 2011;58(1):22-37.
- El Shal S. A Comparative Study of Effect of Intravenous Lidocaine Infusion, Gabapentin and Their Combination on Postoperative Analgesia after Thyroid Surgery. *Open Journal of Anesthesiology*. 2017;7(09):296.

27. Weinberg L, Jang J, Rachbuch C, Tan C, Hu R, McNicol L. The effects of intravenous lignocaine on depth of anaesthesia and intraoperative haemodynamics during open radical prostatectomy. *BMC research notes*. 2017;10(1):248.
28. Honey Parmar D, Kinna Shah D. IMPACT OF INTRAVENOUS LIDOCAINE HYDROCHLORIDE INFUSION IN PERIOPERATIVE ANAESTHETIC CONSUMPTION AND POST-OPERATIVE ANALGESIA.
29. Yon JH, Choi GJ, Kang H, Park J-M, Yang HS. Intraoperative systemic lidocaine for pre-emptive analgesics in subtotal gastrectomy: a prospective, randomized, double-blind, placebo-controlled study. *Canadian Journal of Surgery*. 2014;57(3):175.
30. Wuethrich PY. Intravenous lidocaine and recovery after non-bowel abdominal surgery. *Anesthesia & Analgesia*. 2013;116(4):950.
31. Jendoubi A, Naceur IB, Bouzouita A, Trifa M, Ghedira S, Chebil M, et al. A comparison between intravenous lidocaine and ketamine on acute and chronic pain after open nephrectomy: A prospective, double-blind, randomized, placebo-controlled study. *Saudi journal of anaesthesia*. 2017;11(2):177.
32. Gregory J, Richardson C. The use of pain assessment tools in clinical practice: a pilot survey. *J Pain relief*. 2014;3(2):140-146.