

Comparison of Lidocaine and Tramadol Premedication in Attenuating Propofol Injection Pain at Comprehensive Specialized Teaching Hospital of Ethiopia: A comparative Cross-Sectional Study

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ABSTRACT

Background: Propofol is a widely used drug for the induction of anesthesia and often causes severe, sharp, stinging, or burning pain on the injection that can be distressing to the patient. Premedication with opioids, lidocaine, slow injection, and using a large vein for injection has been tried to combat the problem though there is controversy.

The study aims to assess the effectiveness of intravenous lidocaine and Tramadol in reducing the incidence and severity of pain on Propofol injection for the adult elective surgical patient in Tikur Anbessa Comprehensive Specialized Teaching Hospital, Addis Ababa Ethiopia from February 1, 2018-March 30, 2018. G.C.

Materials and Methods: Comparative cross-sectional study design was employed on a sample of 156 patients divided into two groups of 78. Participants who were 18-60 years old, underwent general anesthesia, and induced with Propofol as well as premedicated with lidocaine or Tramadol were included in the study. Patient interviews, chart review, and pretested questionnaires were employed for data collection. Collected data was analyzed using SPSS version 23. Mann-Whitney U test and chi-square test were used to compare continuous and categorical variables respectively. P-value<0.05 was considered as statistically significant.

Result: The incidence of propofol injection pain after pretreatments with lidocaine (n=78) was 23.1% and the incidence of propofol injection pain after pretreatments with tramadol (n=78) was 34.6% with a p-value of 0.112. The severity of pain expressed in the median and interquartile range of NRS score was 0 (0-2.25) in lidocaine and 0 (0-3) in tramadol group which was comparable between lidocaine and tramadol group with no statistically significant difference between two groups with (P=0.669).

Conclusion: Both Lidocaine and tramadol might reduce the incidence and severity of Propofol injection pain. Anesthetists should consider the use of both lidocaine and tramadol as pretreatment for the attenuation of propofol injection pain.

Keywords: Lidocaine; Propofol injection pain; Premedication

INTRODUCTION

Propofol (2,6-di-isopropyl phenol) introduced clinically in 1977, is an alkyl phenol compound [1]. Currently, it is the most popular intravenous (IV) anesthetic drug especially for briefcases, day surgery, or for laryngeal mask airway insertion. Propofol can be

also used as an anticonvulsant, an antiemetic, in Total Intravenous Technique (TIVA) and critical care units for sedation [2,3]. It has a fast onset and offset with minimal organ toxicity [4-8].

The problem of using propofol is it resulted in severe, sharp, stinging, or burning pain on the injection that can be distressing to

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the patient [9,10]. The mechanism by which Propofol causes pain on injection is not fully understood [11]. The pathophysiology of this pain is proposed to be triggering the local Kallikerin Kinin cascade which induces venous dilation and hyper permeability, thereby probably promoting contact between free Propofol and free nerve endings within the vascular wall, resulting in pain [3,11]. The other suggested mechanism was the stimulation of the nociceptive receptors at the free nerve endings located between the intima and the media layers of the venous wall in which a direct and immediate response is transmitted through the A-delta fibers [7,12] and the PH and concentration nature of the drug could also be the other postulate related to propofol injection-induced pain [3].

The quality of an anesthetic agent is judged by any recall of discomfort or pain at the time of induction [13]. The best intervention to prevent pain on injection with Propofol is unknown [14]. But there are some proposed methods for prevention of Propofol injection pain studied are the site of injection (use of large vein), use of non-steroidal anti-inflammatory drugs, premedication with an opiate, speed of the injection of Propofol, speed of carrier intravenous fluid, the use of local anesthetic (lidocaine), dilution of Propofol, different temperatures, metoclopramide, glyceryl trinitrate, thiopentone and ketamine [15-18]. Pain on injection of Propofol has been reported and is an important limitation of its use and 30% of patients experience severe pain on the injection of Propofol [19,20].

Lidocaine is the most commonly used local anesthetic and it has a relatively short duration of action which limits its postoperative analgesic effect [19]. Pain on injection-induced by propofol is reduced by a preceding injection of lidocaine. Lidocaine pretreatment is the most popular method for reducing this pain though the exact mechanism by which lidocaine reduces pain on injection of propofol is unknown, there is a possibility that lidocaine reversibly blocks peripheral nerve pathways through the action on excitable membranes [9,21].

Tramadol is currently the most commonly prescribed opioid in the world. It is a centrally-acting drug that is effective in the treatment of moderate to severe pain its main acting mechanism is the increase in serotonergic neural conduction; therefore, its analgesic effects can be averted by simultaneous administration of a serotonin-receptor antagonist [21]. Pretreating the vein with IV Tramadol has proved to be effective in preventing Propofol injection pain in adults and the incidence of Tramadol treated patients was 23% [4].

The incidence of pain-induced during Propofol injection has been reported to be 85%-100% [1,10,22,23]. Pain on injection-induced by Propofol is reduced by a preceding injection of lidocaine [24]. Lidocaine pretreatment is the most popular method for reducing this pain [25-28]. However, the failure rate is between 32% and 48% and thus lidocaine may not entirely control Propofol-induced pain [25].

Propofol pain is one of the most ignored, under-diagnosed, and untreated medical problems, particularly in our setup. The question posed regarding the effect of Lidocaine and Tramadol pretreatment has been studied in developed countries by many investigators over the years. There is a controversy regarding the treatment of Propofol injection pain. Some have shown Lidocaine pretreatment is superior to that of tramadol [18]. Some have shown Tramadol pretreatment is also as effective as lidocaine for the prevention of Propofol injection pain [1].

Though the effect of Lidocaine and Tramadol pretreatment in attenuating Propofol injection pain has been studied in developed

countries by many investigators, differences in population, set up and controversy necessitate the current study. There is individual variability in pain perception and recognition due to social, cultural, cognitive, genetic factors, and religious factors [29].

This study is aimed to compare the effectiveness of intravenous lidocaine and Tramadol in reducing the incidence and severity of pain on Propofol injection.

MATERIALS AND METHODS

Study setting and period

This study was done at Tikur Anbessa Comprehensive Specialized Teaching Hospital (TACSTH) from February 1, 2018-March 30, 2018. G.C. It is the largest, multi-specialist tertiary care teaching hospital located in Addis Ababa Capital of Ethiopia. It offers diagnosis and treatment for approximately 370,000-400,000 in a year. It is now the main teaching hospital for clinical and preclinical training in most disciplines. It is also an institution where specialized clinical services that are not available in other public or private institutions are rendered to the whole nation. It has about 800 beds, 17 operation theatre and approximately 7000-9000 patients undergo surgery in a year including emergency surgery.

Study design

A comparative cross-sectional study design was employed at Tikur Anbessa Comprehensive Specialized Teaching Hospital (TACSTH).

Source population

All adult patients who were scheduled for elective general surgeries under GA with ETTI and induced with propofol at TACSTH.

Study population

All adult patients who met inclusion criteria and scheduled for elective general surgeries under GA with ETTI and induced with propofol at TACSTH during the study period.

Dependent Variables

Propofol injection pain

Independent Variables

Age, Sex, ASA status, dose of Propofol, Type of premedication, Dose of premedication and Concentration of Propofol.

Inclusion criteria

Patients scheduled for elective surgery underwent general anesthesia with the induction of Propofol either pretreated with lidocaine or tramadol, Age between 18-60 years and ASA grade I and II.

Exclusion criteria

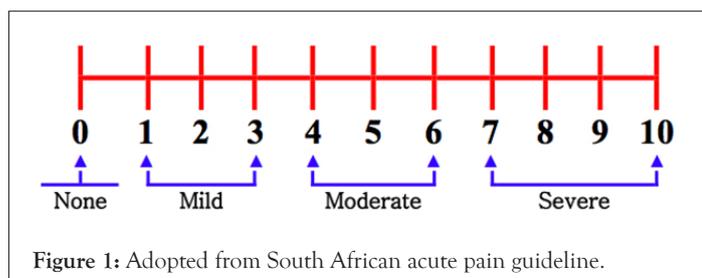
Patients with difficult communication, analgesics premedicated patients, sedative premedicated patients, and patients with a history of neurological or psychiatric disease.

Operational definition

Elective surgery: Scheduled surgeries included non-emergent surgical cases ordered to surgery.

Propofol injection pain: its pain caused after administration of intravenous Propofol.

Numeric rating scale: This is a valid pain intensity assessment tool that involves asking a patient to rate his or her pain from 0-10 (11 point scale) with the understanding that 0 equal no pain and 10 equal the worst possible pain (Figure 1) [30].



SAMPLE SIZE DETERMINATION

The sample size was calculated using a comparison of two proportions with equal sample size formula based on a previous study done in India in 2017 [18] which showed that the incidence of Propofol injection pain in the tramadol group was 25% and in the lidocaine group was 8.3% and using 80% power: A total of 156 adult elective surgical patients were involved in the study.

$$n1 = n2 = \frac{[z\alpha\sqrt{(1+\frac{1}{r})\cdot p^-q^-} + z\beta\sqrt{\frac{p1q1}{r} + p2q2}]^2}{(p1 - p2)^2}$$

Where;

Zα =Standard normal variate for 95% level of significance=1.96

Zβ=Standard normal variate for power of 80% or type 2 error=0.84

p1=the incidence of pain in tramadol group=0.25; q1=1-p1=0.75

p2=the incidence of pain in lidocaine group=0.083; q2=0.917

n1=sample for those patients premedicated with tramadol

n2=sample for those patients premedicated with lidocaine

r=allocation ratio of the sample size=n2/n1=1

p⁻ (change)=(p1+rp2)/1+r=0.1665

q⁻ (change)=1-p⁻=0.8335

$$n1 = n2 = \frac{[1.96\sqrt{1+\frac{1}{1}\cdot 0.1665\cdot 0.8335} + 0.84\sqrt{\frac{0.25\cdot 0.083}{1} + 0.083\cdot 0.917}]^2}{(0.25 - 0.083)^2} = 78$$

Therefore; a total of 156 adult elective surgical patients were involved in the study.

Sampling technique

A study participant was selected using systematic random sampling technique using skip interval from the daily operation in the OR in those patients induced with Propofol and premedicated with lidocaine or tramadol which was used as a sampling frame.

In a situational analysis done for one month, seven patients per day or 147 patients per month underwent surgery-induced with Propofol in TACSTH on average.

Thus, 294 patients were operated on per the study period (2 months). The sampling interval; K was determined using the formula: K=N/n; where, n=total sample size, N=population per 2 months. K=294/156≈2 our skip interval.

Therefore, the sampling interval was two and the first study participant (random start) was selected using the lottery method from the daily operation schedule list. Then, every second case

from the operation schedule were included in the study during the study period. Selected participants were placed in either group based on the anesthetist's premedication plan; whether lidocaine or tramadol. This continues until the desired sample in each group was achieved.

DATA COLLECTION

Data was collected using pretested adapted structured questionnaires by two BSc anesthetists and supervised by one MSc anesthetist. One day training was given for data collectors on the assessment of pain. After providing training for data collectors, written informed consent was taken and data was collected using a structured questionnaire. Socio-demographic data like the patient's age, sex, and ASA physical status, associated coexisting illness was recorded from the chart. The patients were trained on the response of pain using the eleven Point NRS score 0 to 10 in the morning of operation day in the operation room before taking the induction agent. After routine monitoring, (electrocardiogram, noninvasive blood pressure, and pulse oximeter) patients were pretreated with 40 mg of 2% lidocaine and 1 mg/kg tramadol, and simultaneously patients were induced with 2.5 mg/kg of propofol. Propofol injection pain and severity of pain at the induction period were assessed using a numeric rating score as per the protocol prescribed Adopted from South African acute pain guideline scores [30]. Pain scores were assessed during the injection of propofol until the patient asleep based on the patient's complaint.

DATA QUALITY CONTROL

Data was collected using a structured questionnaire prepared in English addressing the objective of the study. The pretest was done on 5% of the sample size at Zewiditu Memorial Hospital. Data collectors and supervisors were trained on each item included in the study tools, objective, relevance of study, right of respondents. During data collection, regular supervision and follow up was made. The investigator cross-checked for completeness and consistency of data on daily basis. Double entry was made on 10% of the sample size.

DATA ANALYSIS AND INTERPRETATION

Descriptive statistics, figures and tables were used to summarize data. The data were checked the normality level with different tests (plot, skewness and kurtosis, curve with histogram and normality test using Shapiro-Wilk and Kolmogorov-Smirnov. However, the data was not normally distributed when checked using all tests and plots. Therefore, a non-parametric alternative, Mann-Whitney U test was used to compare the pain severity, Chi-square (χ²) test was used to analyze the homogenous categorical independent variables and incidence of propofol injection pain between these two groups, but the data was homogeneous as tested by Levene's test of equality of variance. Continuous data was presented as median (IQR) and categorical data was presented by frequencies (percentages), p-value<0.05 was considered as statistically significant.

RESULTS

Socio-demographic characteristics of study participants

A sample of 156 patients included in this study within the age of 18-60 years. Age, sex, ASA status, and BMI were comparable between the groups (Table 1).

Table 1: Socio-demographic characteristic of study participants in Tikur Anbessa Comprehensive Specialized Teaching Hospital, Addis Ababa Ethiopia from February 1, 2018-March 30, 2018.

Variables	Lidocaine	Tramadol	P-Value	
Age in year M (IQR)	37.5 (26-50)	39 (29-55)	0.148	
Sex	Male n (%)	37 (47.4%)	34 (43.6%)	
	Female n (%)	41 (52.6%)	44 (56.4%)	0.63
BMI	<18.5 kg/m ² n (%)	9 (11.5%)	6 (7.7%)	
	18.5-24.9 kg/m ² n (%)	62 (79.5%)	56 (71.8%)	0.109
	25-29.9 kg/m ² n (%)	7 (9%)	16 (20.5%)	
ASA status	ASA I n (%)	59 (75.6%)	54 (69.2%)	
	ASA II n (%)	19 (24.4%)	24 (30.8%)	0.37

Hint M (IQR)=Median and interquartile range, n (%)=Number proportion, Mann-Whitney U test and χ^2 test was used

Type of surgery for propofol Injection

In both groups' majority of patients (59.6%) underwent general surgery and there was no statistically significant difference in the type of surgical procedures done between the groups with a p-value of 0.856 (Figure 2).

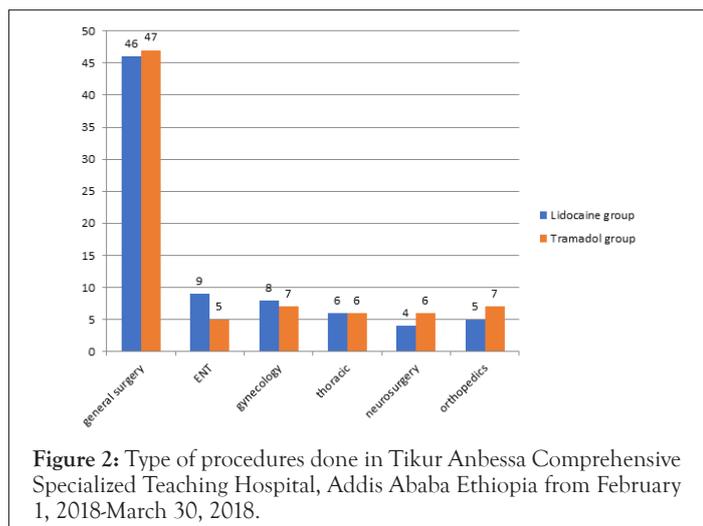


Figure 2: Type of procedures done in Tikur Anbessa Comprehensive Specialized Teaching Hospital, Addis Ababa Ethiopia from February 1, 2018-March 30, 2018.

Incidence of propofol injection pain

The incidence of propofol injection pain was 23.1% and 34.6% for lidocaine and tramadol group which is also comparable p-value 0.112 (Figure 3).

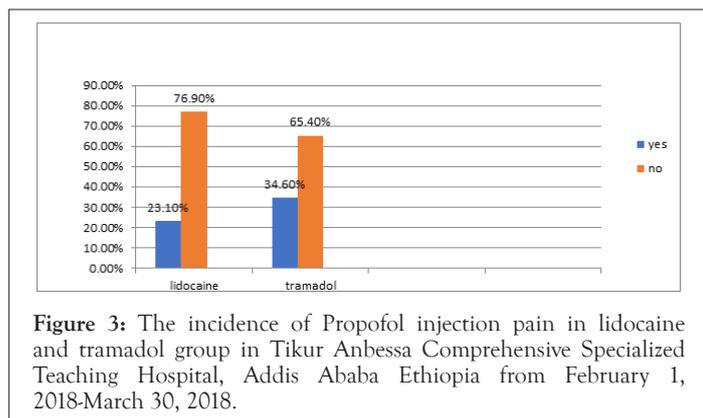


Figure 3: The incidence of Propofol injection pain in lidocaine and tramadol group in Tikur Anbessa Comprehensive Specialized Teaching Hospital, Addis Ababa Ethiopia from February 1, 2018-March 30, 2018.

Severity of propofol injection pain

Pain severity score measured in median and interquartile range of NRS score were 0 (0-2.25) in the lidocaine group and 0 (0-3) in tramadol group which was comparable between the groups with a P-value of 0.669 (Figure 4).

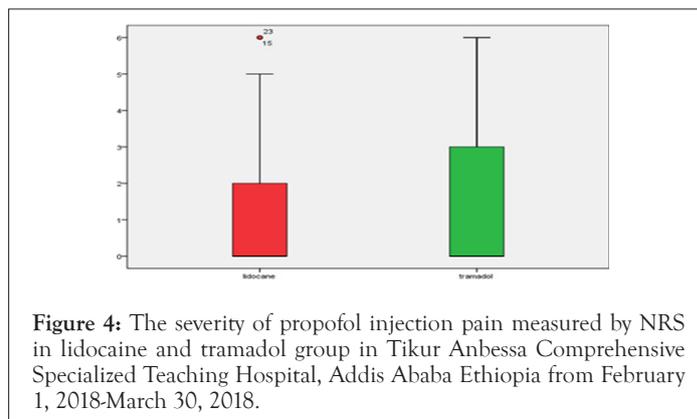


Figure 4: The severity of propofol injection pain measured by NRS in lidocaine and tramadol group in Tikur Anbessa Comprehensive Specialized Teaching Hospital, Addis Ababa Ethiopia from February 1, 2018-March 30, 2018.

DISCUSSION

In our study, there was no statistically significant difference in the incidence of Propofol injection pain after pretreatments with lidocaine and tramadol group which was 23.1% and 34.6% respectively (p=0.112) and there was a reduction in the incidence of pain compared with previous studies reported incidence of propofol injection pain ranging from 85%-100% [1,10,23].

Our result was in line with a prospective randomized open-labeled placebo controlled study conducted by Bashir et al. which found the incidence of pain in patients receiving lidocaine 0.5 mg/kg was 26.7% and in patients receiving Tramadol 1 mg/kg was 30% and there was a significant reduction in the incidence of pain and they concluded that both are equally effective in reducing the incidence of propofol-induced pain (p=0.720) [1].

Similarly, the result of our study is comparable with the studies of Khouadja et al. and Madan et al. in which they reported the incidence of propofol injection pain were 21.7% and 24% respectively after receiving 40 mg of lidocaine as a pretreatment while the incidence of propofol injection pain after tramadol treatment was 28% Madan et al. [23,10].

Our study is inconsistent with the studies done by Zahoor et al. Canbay et al. Nadkarni et al. and Kaya et al. in which they found less propofol injection pain when compared to our study which could be due to, they had applied tourniquet for venous occlusion for 60 seconds, intermittent injection of propofol, and titration of propofol before injection [18,11,2].

In our study the incidence of pain in the lidocaine group was lower compared with a prospective, randomized, double-blind study conducted by Kaya et al. found the incidence of pain on propofol injection in patients pretreated with 20 mg lidocaine without venous occlusion was 45% and there was a statistically significant difference in the incidence of pain in this study with a p-value of 0.05) [16]. The likely explanation for the difference could be due to the lower dose of lidocaine they administered.

In our study there was no statistically significant difference in the severity of Propofol injection pain after pretreatments with lidocaine and tramadol group with of P-value of 0.669 which is in line with a prospective randomized study conducted by Bashir et al. and Khouadja et al. as they found there was no statistically significant difference between lidocaine and tramadol group in

the severity of propofol injection pain a p-value of >0.05 [1,23]. While our study inconsistent with researches done by Zahoor et al. Canbay et al. and Nadkarni et al. as they found there is a statistically significant difference between the groups regarding propofol injection pain severity p-value <0.05 . The decrement in the severity of pain in these studies probably due to the application of a tourniquet and venous occlusion after giving of the pretreatment drugs, intermittent injection, and titration of propofol [18,11,2].

In our study, the severity of pain in the lidocaine group was a lower compared to study done by Kaya et al. in Turkey found the severity of pain on propofol injection in patients pretreated with 20 mg lidocaine without venous occlusion with a p-value of 0.05 [16]. The likely explanation for the difference could be due to the lower dose of lidocaine they were administered.

CONCLUSION

The result of this study indicated that both lidocaine and tramadol might reduce the incidence and severity of Propofol injection pain. The choice of agent should be individualized with due consideration to the cost-effectiveness and benefit to the patient.

RECOMMENDATION

Anesthetists should consider the use of both lidocaine and tramadol as pretreatment for the attenuation of propofol injection pain.

LIMITATION OF STUDY

It is a single-center study.

STRENGTH OF STUDY

The study participants were homogenous.

AVAILABILITY OF DATA

Data are available from the corresponding author based on reasonable request.

COMPETING INTERESTS

No

AUTHORS' CONTRIBUTIONS

Metages Hunie developed the proposal, collected the data, analyzed the data, and prepared the manuscript. Mulualem Sitot, Woseneleh Admasu, Efreem Fenta, Amanu Gashaw and Diriba Teshome revised the proposal, involved in data collection, data analysis, and manuscript preparation.

ETHICAL APPROVAL

Ethical clearance was obtained from Addis Ababa University's ethical clearance committee and Confidentiality of the information was assured by using code numbers than personal identification like names and keeping questionnaires locked in a secured place.

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