Addis Ababa University
አዲስ፡አበባ፡ዩኒቨርሲቲ
Seek Wisdom, Elevate your Intellect and Serve Humanity

COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE

Comparative Study between Intravenous Lidocaine and Fentanyl in Attenuating Cardiovascular Response To laryngoscopic Intubation in Adult Patients Undergoing Elective Surgery in Tikur Anbessa Specialized Hospital

A Thesis to Be Submitted to Addis Ababa University School of Medicine in Partial Fulfillment for the Requirement of Specialty Certificate of Anesthesiology ,critical care and pain medicine(ACCPM)

By; Dr. Mezmure Kenea

April 30, 2024

Addis Ababa, Ethiopia

Comparative Study between Intravenous Lidocaine and Fentanyl in Attenuating Cardiovascular Response To laryngoscopic Intubation in Adult Patients Undergoing Elective Surgery in Tikur Anbessa Specialized Hospital

Principal investigator:

Dr. Mezmure Kenea (ACCPM resident at Addis Ababa University College of health science)

Advisors:

Dr. Rahel Tilahun (MD, consultant anesthesiologist and cardiothoracic anesthesiologist at Addis Ababa University College of health science)

Dr. Tseganesh Birhanu (MD, consultant anesthesiologist at Addis Ababa University College of health science)

April 30, 2024

DECLARATION OF THE PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical Conduct of the research project and for provision of required progress reports as per terms and Conditions of the Department and College, in effect at the time of grant is forwarded as the Result of this application.

Name of the student: Dr. Mezmure Kenea

Date: April 30, 2024 Signature _________________

APPROVAL OF THE FIRST ADVISOR

Name of the first advisor: Dr. Rahel Tilahun

Date: April 30, 2024 Signature _________________

APPROVAL OF THE SECOND ADVISOR

Name of the second advisor: Dr. Tseganesh Birhanu

Date: April 30, 2024 Signature _________________

Statement of declaration

I hereby declare that this research thesis is my original work and has not been presented by any other individual in any of the universities in Ethiopia. All sources of materials used for this thesis have been duly acknowledged.

Name: Dr Mezmure Kenea

Signature:

Date: April 30, 2024

This research thesis has been submitted for examination with my approvalas research advisor

Name of the first advisor: Dr. Rahel Tilahun

Signature:

Date:

Name of the second advisor: Dr. Tseganesh Birhanu

Signature:

Date:

Acknowledgement

My deepest gratitude goes to Dr. Rahel Tilahun and Dr. Tseganesh Birhanu for their support during this document preparation and also I would like to thank Addis Ababa University School of Medicine for giving me this opportunity.

Table of Contents

Acknowledgement 5
List of tables and figures 8
Abbreviation and Acronomy 9
Abstract 10
Background: 10
Objective 10
Method: 10
Result 10
Conclusion: 10
1. Introduction 1
1.1 Background 1
1.2 Statement of the problem 2
1.3 Significance of the study 3
2. Literature review 5
3. Objective and hypothesis 9
3.1 General objective: 9
3.2 Specific objectives: 9
4. Hypothesis 10
5. Method 11
5.1 Study design 11
5.2 Study area and period 11
5.3 Populations 11
5.3.1 Source population 11
5.3.2 Study population 11
5.4 Inclusion and exclusion criteria 11
5.4.1 Inclusion criteria 11
5.4.2 Exclusion criteria 12
5.5. Sample size 12
5.6 sampling procedure 13
5.7 study variable 13

5.7.1 Independent variable ... 13
5.7.2 Dependent variable ... 13
5.8 Data collection procedure ... 13
5.9 Data analysis and interpretation ... 14
5.10 Ethical consideration ... 14
5.11 Dissemination plan ... 14
5.12. Operational definitions ... 14
6. Result ... 16
6.1 Demographic and clinical characteristics of the study participants between groups ... 16
6.2 Comparison of base line hemodynamic parameters between fentanyl and lidocaine group ... 17
6.3 Comparison of change in HR from base line between groups ... 18
6.3 Comparison of change in SBP from base line between fentanyl and lidocaine ... 19
... 20
6.4 Comparison of change in DBP after intubation from base line between lidocaine and fentanyl ... 20
6.5 Comparison of change in mean arterial blood pressure from base line ... 21
7. Discussion ... 23
8. Strength and limitation ... 25
9. Conclusion and recommendation ... 26
9.1 conclusion ... 26
9.2 recommendation ... 26
Reference ... 27
Annex ... 30
Annex 1: Questioner ... 30
Annex 2: Subject information sheet ... 32
Annex 3: informed consent form ... 33

List of tables and figures

List of tables

- Table 1. The sociodemographic characterstics of the participants within each group
- Table2. The baseline hemodynamic parameter between the fentanyl and lidocaine group
- Table 3. The mean and SD of HR values among the two groups across different time frames
- Table 4. The mean and SD values of SBP among the two groups across different time frames
- Table 5.The mean and SD of DBP values among the two groups across different time frames
- Table 6. The mean and SD of MAP values among the two groups across different time frame

List of figure

- Figure1. The distribution of the type of surgery among the two groups.
- Figure 2. Mean HR between fentanyl and lidocaine at baseline,1st, 3rd,5th minute
- Figure 3. Mean SBP between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute
- Figure 4 Mean DBP between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute
- Figure 5. Mean MAP between fentanyl and lidocaine at baseline,1st, 3rd,5th minute

Abbreviation and Acronomy

ACCPM: Anesthesiology, Critical Care and Pain Medicine

ASA: American Society of Anesthesiology

TASH: Tikur Anbessa Specialized Hospital

RCT: randomized control trial

OR: Operation Room

BP: blood pressure

MAP: Mean Arterial Pressure

HR: Heart Rate

SBP: Systolic Blood Pressure

DBP: Diastolic Blood Pressure

SPSS: Statistical Package for Social Sciences

ETB: Ethiopian Birr

GA: General Anesthesia

ETT: Endotracheal Tube

Torr: 1 torr=1 mmgh

IV: intravenous

SD: standard deviation

Abstract

Background: Endotracheal intubation is done for various indications and maintaining the airway during general anesthesia is one of them. Though intubation is seldom eventful in a healthy individual with no comorbidity, it can complicate patient's condition if the procedure isn't smooth. So blunting hemodynamic responses due to the laryngoscopy and intubation is recommended during these procedures. Several pharmacologic agents have been recommended such as: opioids, local anesthetics, beta blockers and deepening inhalational agents. This study tries to compare fentanyl and lidocaine in attenuating those hemodynamic responses.

Objective: To compare the effectiveness of fentanyl and lidocaine in attenuating hemodynamic response to laryngoscopy and intubation in Tikur Anbessa specialized hospital.

Method: Institution based randomized control trial was be done in Tikur Anbessa specialized hospital from July 1 to September 30. 86 Patients were assigned into two groups: 43 patients were assigned as Group F and as Group L. the fentanyl group were given 2μ/kg and the lidocaine group took 1.5 mg/kg (2%). Data was collected from the chart and observation of the anesthesia monitor. Data was personally verified for accuracy before being coded and placed into SPSS. With the aid of the computer program SPSS version 25, data was cleaned and examined. The analysis was done using chi square test for the socio demographic data and independent t test was used to assess the mean and standard deviation for the two groups of the participants. For all analyses, a P value of 0.05 or lower is regarded as statistically significant.

Result: there was no significant difference between the groups in regard to socio demographic data and baseline hemodynamic parameters. The mean and SD of the1st minute HR is 93.65+12.32 and 98.23+10.19 for fentanyl and lidocaine respectively. The p value of the first minute HR between the two groups is 0.064. There is no significant difference between the groups at 1st, 3rd and 5th minute. There is significant difference regarding the first minute SBP, DBP and MAP with a p value of < 0.05. Otherwise the p value for third and fifth minute is insignificant.

Conclusion: the blunting capacity of fentanyl is superior to lidocaine especially on the hypertensive response to laryngoscopic intubation of the first minute. Even though the result doesn't indicate significance, the HR response is better attenuated with fentanyl.

1. Introduction

1.1 Background

Endotracheal intubation is a routine procedure performed in various occasions when definitive airway is mandatory. Unfortunately, it results in a cascade of physiologic and pathophysiologic reflex responses(1). Proprioceptors located in the trachea and supraglottic area trigger the cardiovascular reactions to noxious airway manipulation and tissue irritation.

The most typical reaction to airway manipulation in adults and adolescents is tachycardia and hypertension, which are mediated by the sympathetic chain ganglia and cardioaccelerator nerves.(2). This reaction involves the adrenal medulla secreting adrenaline and the adrenergic nerve terminals releasing norepinephrine widely. The renin-angiotensin system is also partially responsible for the hypertensive reaction after endotracheal intubation (1). Pressor responses during intubation result from both stimulation by direct laryngoscopy and placement of the tracheal tube(3). The rapid rise in arterial blood pressure and heart rate (HR) that characterizes the pressor reaction, occurs 30 seconds after laryngoscopy and intubation and gradually decreases to baseline levels in 5–10 minutes.(4).

EEG activity, cerebral blood flow, and cerebral metabolic rate increase show that laryngoscopy and endotracheal intubation stimulate the central nervous system in addition to the autonomic nervous system.(2). In a healthy person, these pathophysiologic reactions are more or less bearable, but in patients with heart illness or myocardial ischemia, an aortic or cerebral aneurysm, increased intracranial pressure, or arteriovenous malformation, these reactions may be harmful. These modifications may lead to herniations, intraoperative myocardial ischemia, arrhythmias, acute decompensated heart failure, and intracranial hemorrhage.

Numerous trials have been carried out to decrease this hemodynamic response to laryngoscopy and intubation. Vasodilators such as hydralazine, sodium nitroprusside and nitroglycerin have been tried. Additionally topical lignocaine anesthetic for the oropharynx (viscous), intravenous lignocaine, adrenergic blocking drugs (either alpha or beta blockers), deep inhalational anesthesia, and intravenous opioids are some examples of these. It has not been determined which agent is the most suitable for this use(5).

Reid and Brace made the first attempts to comprehend the hemodynamic alterations brought on by intubation in 1940. In 10 out of the 35 individuals they looked at, they discovered extrasystoles in the auricle and the ventricle, a delayed conduction time, and slowing of the heart. The authors hypothesized that the mechanical stimulation of the laryngotracheal mucosa by the endotracheal tube caused these alterations, which in turn triggered the vagus nerve.(6). Since this time, numerous researchers have worked to understand these hemodynamic alterations and possible preventative strategies.

Lidocaine is a low-potency, rapid-onset, and intermediate-acting amide local anesthetic. Local anesthetics bind to closed, inactivated sodium channels and prevent subsequent channel activation. Since sodium cannot pass through closed, inactivated sodium channels, action potentials cannot be produced. Fentanyl is a strong synthetic narcotic analgesic with quick onset and brief duration of action. This synthetic opioid agonist, which is low molecular weight and highly lipid soluble, is widely employed as an intravenous analgesic supplement, inhalation component, balanced anesthesia, neuroleptic analgesia, and as a sole anesthetic. Its analgesic potency is 75–125 times greater than that of morphine. After intravenous administration, the onset of effect is 1-2 minutes, and the duration is 1 hour. As such, it has demonstrated to be optimal for managing the transient hemodynamic consequences linked to laryngoscopy and intubation.(5).

1.2 Statement of the problem

Direct laryngoscopy and tracheal intubation are performed for multiple reasons, and understanding their pathophysiologic responses is crucial in managing patients, especially those who have comorbidities. The pressor response elicited by laryngoscopy alone is nearly identical to that produced by laryngoscopy plus intubation. It begins in five seconds, peaks in one to two minutes, and then settles back to the baseline in five minutes(7). Hypertension and tachycardia are the most common manifestations of these procedures. Though these responses are tolerable in healthy individuals, they have grievous consequences in cardiac and neurosurgical patients. So hindering these responses is necessary whenever we are performing those procedures.

Various pharmacologic drugs have been suggested as cardiovascular blunting agents, and among those, intravenous fentanyl and lidocaine are commonly utilized medications during the induction of general anesthesia.

1.3 Significance of the study

One of the quality of care indicators is safety of the patient during induction of anesthesia and it is crucial to optimize the perioperative period. One of the crucial procedures when administering general anesthesia is intubation. The hemodynamic changes during intubation can determine patient outcome in the perioperative period(8). It is currently uncertain what exact mechanism causes the hemodynamic response to laryngoscopy and intubation. Reports have connected it to elevated plasma concentrations of catecholamines, primarily norepinephrine and to a lesser extent epinephrine. Blunting the cardiovascular hemodynamic response using different pharmacologic medications has been suggested. In TASH, intravenous lidocaine and fentanyl are used during direct laryngoscopy and intubation. In order to lessen the stress reaction to the intubation, these drugs are given either alone or in combination(9).

In TASH, we encounter various patients who require general anesthesia to undergo a procedure. Optimizing the induction time is part of our duty as anesthesia practitioners to ensure the safety of our patients, particularly for those who do have underlying comorbidities like cardiac and neurological disorders.

Even though this study is focused on patients undergoing general anesthesia, this outcome might give us insight into any patient undergoing intubation, including those in intensive care units and emergency care units. In these settings, we encounter a handful of patients who have a critical illness that may require intubation and ventilation. So this study can give us insight regarding blunting hemodynamic responses to laryngoscopy and intubation.

Many anesthesia providers have been interested in cardiovascular reactions to laryngoscopy and tracheal intubation for many years. Awareness has been created that the common occurrence of tachycardia, hypertension, and arrhythmia after this, regular anesthetic procedure may be harmful. In addition to this unexpected mortality can occur shortly after and during intubations(10).

Though there have been many studies done regarding these harmful effects of intubation all over the world, the results are contradictory. In our setup, the available and commonly suggested drugs are fentanyl and lidocaine. There are two studies done in our country focusing on these drugs. The first one was published in 2019 in TASH, and the second one was published in 2020 in Dilla University Hospital. Even though these publications have suggested similar results, many studies that have been done in this area in other countries are contradictory. My research consolidate the results of the above two studies and also create a space for more advanced study in the field.

2. Literature review

It is common knowledge that patients with coronary artery disease, systemic arterial hypertension, aneurysmal vascular disease, and poor intracranial compliance run the risk of experiencing life-threatening consequences as a result of laryngoscopy and tracheal intubation(11). Many researchers have done studies regarding the prevention methods of this pathophysiologic reflex using different pharmacologic agents. Ventricular arrhythmias and changes to the ST-segment have been linked to post-intubation pressor responses. The levels of catecholamines changes greatly. The levels of norepinephrine may double and last for 5-8 minutes, while the levels of adrenaline may quadruple.(6).

Stoelting did a study in 1977 to understand the circulatory response to laryngoscopy and tracheal intubation with or without prior oropharyngeal viscous lidocaine. He did his research on 20 adult patients undergoing elective aortocoronary vein bypass grafts and compared them to a control group that didn't take oropharyngeal lidocaine. Compared with control patients, MAP increased less in response to tracheal intubation (23 ± 5 torr versus 39 39± 4 torr, $p < 0.05$) and returned toward awake levels sooner in patients receiving viscous lidocaine. HR increased about 20 bpm ($p<0.05$) with or without viscous lidocaine(12).

Martin has published a study on 36 patients undergoing major vascular surgery for their response to tracheal intubation in 1982. These patients were assigned randomly to receive thiopental (3 mg/kg) and fentanyl (8μg/kg) along with thiopental only (6 mg/kg) (18 patients). ECG, blood pressure, pulmonary capillary wedge pressure, central venous pressure, and cardiac output were measured during induction, laryngoscopy, and intubation. MAP increased more following intubation in patients given thiopental than in patients given fentanyl and thiopental, reaching a peak value of 144± 4 torr in patients receiving thiopental only, compared with 108 ± 6 torr in those receiving fentanyl and thiopental ($p<0.0001$). The HR increased slightly with induction of anesthesia, and following intubation, the absolute value of the heart rate was significantly greater after thiopental than after fentanyl and thiopental ($p < 0.05$) (13).

Feng and Chan did a randomized, single-blinded study in 1996 comparing lidocaine, fentanyl, and esmolol for attenuation of the cardiovascular response to laryngoscopy and tracheal intubation. 80 ASA class I or II patients undergoing elective, non-cardiac procedures were included in the study, which consisted of 4 groups: group A received normal saline as a control, while group B, group C, and group D received lidocaine (2 mg/kg), fentanyl (3μ/kg), and esmolol (2 mg/kg), respectively. HR and SBP were obtained every minute for 10 minutes after induction. After intubation, the incidence of tachycardia (HR > 100/min) was found in 15% of patients in the esmolol group, significantly lower than 85% of patients in the control group, 75% of patients in the lidocaine group, and 55% of patients in the fentanyl group, respectively (p <0.05). The incidence of hypertension (SBP > 180 mmHg) was found in 20% of patients in the esmolol group, significantly lower than 80% of patients in the control group, 70% of patients in the lidocaine group, and 40% of patients in the fentanyl group (p <0.05)(14).

College of Medical Sciences and Hospital, Karnataka, India did a RCT in 2018 regarding intravenous fentanyl and lidocaine in attenuating hemodynamic response to intubation. Ninety patients who were scheduled for elective procedures which had ASA classes I and II were chosen at random and split into three groups of thirty. Group 1(lignocaine 1.5 mg/kg), Group 2 (fentanyl 2 μg/kg), and Group 3 (control, received normal saline). Comparing the fentanyl group to the lignocaine (33%) and control (42.5%) groups, there was a statistically significant decrease in heart rate rise (26%) (P = 0.018). At intubation, the lignocaine group experienced a lower rise in systolic blood pressure (14.5%) than the control group (20%) (P = 0.000).

. Group 1 (control-received normal saline), Group 2 (Lignocaine 1.5 mg/kg), and Group 3 (Fentanyl 2 μg/kg). The fentanyl group showed significantly lesser rise (26%) in heart rate compared to lignocaine (33%) (*P* = 0.018) and control group (42.5%) (*P* = 0.000). The lignocaine group showed lesser rise in systolic blood pressure (14.5%) compared to control group (20%) (*P* = 0.000) at intubation(6).

In 2017, Mashhad University of Medical Sciences, Iran, did a study on the effects of intravenous administration of fentanyl and lidocaine on hemodynamic responses following endotracheal intubation. They included 96 patients who needed RSI in the emergency department, and they were randomly divided into three groups (fentanyl group (F), lidocaine

group (L), and fentanyl plus lidocaine (M) as their control group). M was administered with 3 µg/kg fentanyl and 1.5 mg/kg of lidocaine; F was injected with 3 µg/kg fentanyl; and L received 1.5 mg/kg lidocaine prior to endotracheal intubation. HR and MAP were assessed four times: before, immediately after and 5 and 10 minutes after intubation. HR was notably different in the F, L, and M groups during the four time courses ($p<0.05$). Comparison of MAP at measured points in all groups exhibited no significant difference ($p>0.05$). This study shows that lidocaine effectively prevents MAP and HR fluctuations following the endotracheal intubation(15).

In Basrah teaching hospital, an RCT was done comparing intravenous lidocaine and fentanyl after propofol induction during laryngoscopy and intubation. They included 60 patients, which were again divided into three groups of 20 patients. The first group received 10 ml of normal saline, the second received a 2µg/kg intravenous bolus of fentanyl, and the third received a 1.5-mg/kg lignocaine injection 3 minutes before laryngoscopy and intubation. As a baseline record, HR and BP were taken noninvasively upon entry to the theater, immediately following induction, and then 1, 3, 5, 7, and 10 minutes after intubation. There was no discernible difference between lignocaine and fentanyl in their ability to prevent an increase in HR during laryngoscopy and intubation ($p > 0.05$). Both fentanyl and lignocaine were equally successful in preventing a significant increase in SBP, DBP, and MAP(16).

RCT was done on patients undergoing elective surgery in Dilla, Ethiopia, in 2020. The study examined the effects of intravenous fentanyl and lidocaine on the hemodynamic response to endotracheal intubation and laryngoscopy. 52 patients were in the study, which were categorized into two groups: 26 of them took 2µg/kg of fentanyl, and 26 of them were given 1.5 mg/kg of lidocaine. The hemodynamic variables were recorded at the 1st, 3rd, 5th, and 10th minutes of intubation. The mean rise in HR from baseline was higher in the lidocaine group (29.26 ± 15.02 bpm) compared with the fentanyl group (17.56 ± 10.28 bpm) at the 1st minute. The mean rise in SBP from baseline at the 1st minute is lower in the fentanyl group (17.53 ± 13.04) compared with the lidocaine group (31.53 ± 17.24). At the third, fifth, and tenth intervals, the mean increase in hemodynamic variables from the baseline was similar among groups (P value > 0.05)(17).

A comparative cohort study was done at Addis Ababa University, TASH, in 2019 to assess the effectiveness of fentanyl and lidocaine in attenuating the cardiovascular response to laryngoscopic intubation in elective surgical patients. The study included 114 patients, and they were grouped into two groups. The fentanyl group took 2 mg/kg, and the lidocaine group took 1.5 mg/kg, 3 minutes prior to intubation. HR, DBP, and SBP were recorded prior to induction, at the 1st minute, 3rd minute, and 5th minute after intubation. The mean HR at the first minute after intubation was significantly lower in the fentanyl group (98.91 $\pm$ 15.6 bpm) compared to lidocaine (107 $\pm$ 15.45 bpm), $p = 0.006$. SBP was also significantly lower in the fentanyl group (141.9 $\pm$18.9 mmHg) compared to lidocaine (150 $\pm$18.098 mmHg), $p = 0.016$ at the 1st minute after intubation. At the 3rd minute after intubation, the HR was significantly lower in the fentanyl group compared to lidocaine ($p = 0.037$). No difference was observed in HR and BP among the group at the 5th minute after intubation ($p > 0.05$) (18).

The studies have tried to compare fentanyl and lidocaine in attenuating the hemodynamic responses to laryngoscopic intubation. Some of them suggest fentanyl is superior to lidocaine, and the others say they are equal or that lidocaine is superior. Fentanyl appears to be a better option than lidocaine, according to study conducted in Ethiopia; nonetheless, there are several shortcomings that may be addressed. The sample size is smaller in one study, and both studies didn't limit the time duration or the trial of the laryngoscopy. It is a fact that the trial will have many limiting factors that will alter the power of the study. So these factors should be considered in the analysis part of the research. Since the accessibility of drugs, especially fentanyl, is difficult here in Ethiopia most of the time, it is helpful if we have an understanding of which of the two is most effective in blunting the cardiovascular response. The study will also have an impact on enforcing some regulations regarding induction medications. In addition to this, it will encourage the hospital pharmacy unit to avail the drug that is most effective in attenuating pathophysiologic responses that will be devastating in some patients with comorbidities.

Some of the research mentioned above has its strengths and weaknesses. Most of them are randomized and double-blinded, which greatly increases reliability. Three of the studies we reviewed here used normal saline as a control group, which might have a huge ethical issue in the trial, though it increased its significance. Our study didn't involve a control group that was used by some of the researchers.

3. Objective and hypothesis

3.1 General objective:

- To compare intravenous fentanyl and lidocaine in blunting hemodynamic responses to direct laryngoscopy and intubation in elective surgical patient undergoing general anesthesia at TASH, Addis Ababa, Ethiopia, in 2023

3.2 Specific objectives:

- To compare intravenous lidocaine and fentanyl on attenuation of heart rate in response to direct laryngoscopic intubation.
- To compare intravenous lidocaine and fentanyl on attenuation of blood pressure in response to direct laryngoscopic intubation.

4. Hypothesis

H1. There is no significant difference among patients who took intravenous fentanyl and lidocaine in blunting hemodynamic response during direct laryngoscopy and intubation

H2. There is significant difference among patients who took intravenous fentanyl and lidocaine in blunting hemodynamic response during direct laryngoscopy and intubation.

5. Method

5.1 Study design

It is an institution based single blinded randomized control trial.

5.2 Study area and period

This study was conducted in the elective operating theaters of Tikur Anbessa specialized hospital, Addis Ababa, Ethiopia. It is one of the largest referral hospitals in the country, and it also accommodates both undergraduate and postgraduate trainees in clinical as well as preclinical disciplines. Between September 2010 and September 2015, 8,698 surgical admissions were made at the institution, which means an average of 1,740 admissions per year. Of these, 54.1% were elective surgeries, and 44.9% were emergency surgeries(19). The hospital has 12 operating theaters, which include 9 in the main operation room, 1 in the obstetric unit, and 2 in the orthopedic unit. The study took place from July 1 to September 30, 2023.

5.3 Populations

5.3.1 Source population

All adult patients who were scheduled to have elective procedures performed in the Tikur Anbessa specialized hospital under general anesthesia with direct laryngoscopic intubation.

5.3.2 Study population

The study included all adult patients who underwent elective procedures during the study period under general anesthesia with direct laryngoscopic intubation and those who met the inclusion criteria.

5.4 Inclusion and exclusion criteria

5.4.1 Inclusion criteria

- Age >18 years

- ASA class 1 and 2

5.4.2 Exclusion criteria

- Anticipated difficult airway patients
- Patients on regular medication which affect HR or BP
- Obstetric patients
- Neurosurgical patients
- Cardiac patients
- Arrhythmia
- More than one trial and laryngoscopic time >20 second

5.5. Sample size

Sample size was calculated using Epi Info software version 3 using two mean difference comparisons, using a previous study done in India(6). The study showed a mean SBP of 149± 18.98 for the lidocaine group and 140.37±10.39 for the fentanyl group at the first minute of intubation. With a 5% significance level, a 95% confidence level (standard value of 1.96), and an 80% power, this formula is used.

$$n = \frac{(S_1^2 + S_2^2)(Z\ \ /2 + Z\ \ )^2}{(u_1 - u_2)^2}$$

Where

$Z\ \ /2 = 1.96$ for a $p = 0.05$ (95% confidence interval)

$Z\ \ = 0.84$ for 20% beta error

S = standard deviation

μ= SBP mean

$$n = \frac{(18.98)^2 + (10.39)^2\ (1.96 + 0.84)^2}{(149 - 140.37)^2}$$

n = 42 in each group, and adding a 10 % non-respondent rate, the total sample size will be 90 which is 45 patients will be included in the study.

5.6 sampling procedure

Simple random sampling taken from the sampling frame was done via lottery method.

5.7 study variable

5.7.1 Independent variable

- Age, sex, weight
- ASA class
- MG
- Anesthetic blunting agent

5.7.2 Dependent variable

- HR
- MAP
- SBP
- DBP

5.8 Data collection procedure

Data was collected via a structured questionnaire by the anesthesia provider team after information is provided on how to fill out the questionnaire appropriately. Both chart review and information from observation was recorded to fulfill the question. Demographic, surgical, and anesthesia-related information entries was copied from the chart. Whereas the hemodynamic variables (HR, MAP, SBP, and DBP) were recorded from the anesthesia monitor at pre-intubation time (baseline) and then at the 1st, 3rd, and 5th minutes after intubation. The patients who received 2μg/kg of fentanyl was assigned to group F, and the patients who received 1.5 mg/kg of lidocaine was assigned to group F. These medications were given 3 minutes before intubation, and after intubation, any form of procedure such as catheterization and painful interventions were restricted.

5.9 Data analysis and interpretation

The data was personally verified for accuracy before being coded and placed into SPSS version 25.the data was cleaned and examined. Utilizing the Shapiro-Wilk test and a histogram with an overlaid curve, it was determined whether the data were distributed normally.

The analysis was done using chi square test for the socio demographic data and independent t test was used to assess the two groups of the participants. The data were presented as the mean standard deviation. For all analyses, a P value of 0.05 or lower is regarded as statistically significant. Data, tables, and figures were compiled using descriptive statistics to present the results.

5.10 Ethical consideration

A support letter was obtained from Addis Ababa University College of Health Science, Department of Anesthesiology, Critical Care, and Pain Medicine. Each participant gave verbal informed consent after being told of the study's objectives and significance. An anonymous questionnaire was used throughout the entire investigation to guarantee confidentiality, and all responses were kept anonymous and confidential.

5.11 Dissemination plan

The study result will be submitted to Addis Ababa University College of Health Sciences, Department of Anesthesiology, Critical Care, and Pain Medicine. A great effort will be made to publish the findings in the International Journal of Anesthesia.

5.12. Operational definitions

Intubation: a process whereby the health provider inserts a tube through a person's mouth or nose, then down to the trachea.

Laryngoscopy: a procedure to examine the interior of the larynx using a device called a laryngoscope

Endotracheal tube: plastic tube that will be placed in the trachea and used to secure the airway.

Laryngoscopic intubation (LI): Insertion of a flexible tube through the trachea by using a laryngoscope

Hemodynamic presser response: It is defined as a 20% rise in hemodynamic parameters (HR and BP) from the baseline(20).

Fentanyl 2 µg/kg: the recommended intravenous dose during induction of anesthesia to blunt the hemodynamic pressor response to laryngoscopy and intubation.

Lidocaine (2%) 1.5 mg/kg: Intravenous recommended dose to blunt the hemodynamic pressor response to laryngoscopy and intubation.

ASA I: A person in good health. A person who doesn't smoke tobacco products and minimally uses alcohol.

ASA II: A patient with mild systemic disease. Mild diseases only without substantive functional limitation. Current smoker, social alcohol drinker, pregnancy, obesity (30<BMI<40), well-controlled DM/HTN, mild lung disease.

6. Result

6.1 Demographic and clinical characteristics of the study participants between groups

From the 90 participants 4 of them were withdrawn due to violation of protocol. The study included 86 patients, whose sociodemographic details are displayed in the table below.

Forty three patients took fentanyl and the other forty three patients took lidocaine as airway blunting anesthetic agent prior to laryngoscopy and intubation. There is no statistical significance between the two groups regarding age, sex, weight, ASA class, MG and the type of surgery. The mean age for the fentanyl and lidocaine group is (35.77+12.739) and (39.51+13.578) respectively with a P value of > 0.05. There are 24 female and 19 male participants in the fentanyl group: where as in the lidocaine group 21 participants are female and 22 were male. The gender of patients was statistically insignificant with a p value of 0.517 using chi-square test. The mean weight of the fentanyl and lidocaine group were (62.30+10.507) and (60.44+11.031) respectively with a p value of >0.05 using independent sample t test. The ASA class and the MG class also had a p value of > 0.05. The type of surgery that the two group had is depicted with the bar chart below with no significant difference.

Figure1. The distribution of the type of surgery among the two groups.

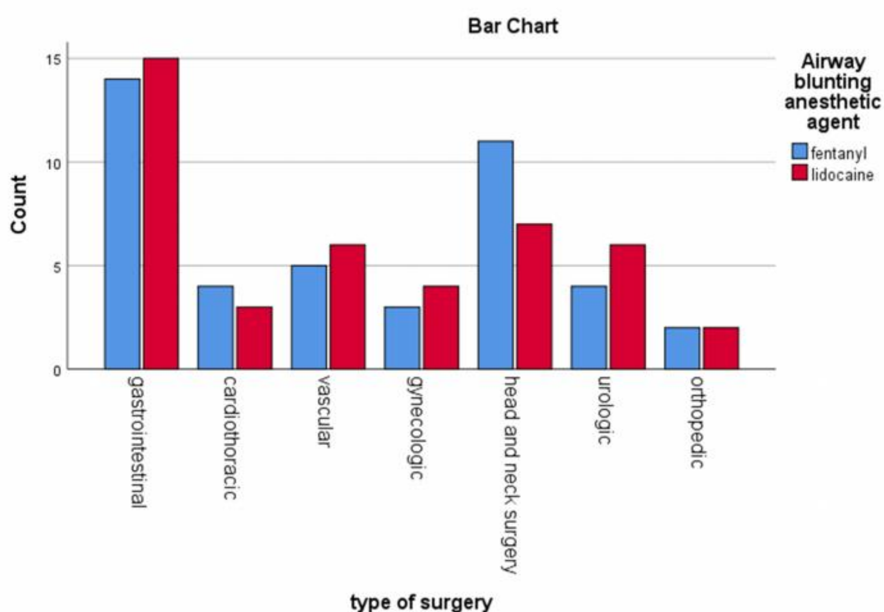


Table 1. The sociodemographic characterstics of the participants within each group

	Fentanyl	Lidocaine	P value
Age(Mean±SD)years	35.77+12.739	39.51+13.578	0.191
Sex(F/M) %			
Female	24(55.8)	21(48.8)	0.517
Male	19(44.2)	22(51.2)	
Weight(KG) Mean±SD)	62.30+10.507	60.44+11.031	0.426
ASA(I/II)			
ASA I	24(55.8)	26(60.5)	0.662
ASA II	19(44.2)	17(39.5)	
MG(I/II)			
MG I	25(58.1)	23(53.5)	0.664
MG II	18(41.9)	20(46.5)	
Type of surgery			
Gastrointestinal	14(34.9)	15(32.6)	
Cardiothoracic	4(7)	3(9.3)	
Vascular	5(11.6)	6(14)	
Gynecology	3(7)	4(9.3)	
Head And Neck	11(25.4)	7(16.3)	0.945
Urologic	4(9.3)	6(14)	
Orthopedic	2(4.7)	2(4.7)	

6.2 Comparison of base line hemodynamic parameters between fentanyl and lidocaine group

The baseline hemodynamic parameters were taken from the study participants before any form of drugs or procedures were done using a pulse oximeter, noninvasive BP cuff and ECG. The

mean and standard deviation is used to compare the variance between the groups using independent t test.

As shown in the table below there is no significant difference with their base line HR and BP between the two groups

Table2. The baseline hemodynamic parameter between the fentanyl and lidocaine group

	Fentanyl	Lidocaine	P value
Baseline HR	79.37±10.42	82.16±9.409	0.196
Baseline SBP	121.67+10.327	123.14+12.338	0.552
Baseline DBP	73.42+13.772	75.16+12.329	0.538
Baseline MAP	83.77+9.486	86.79+13.611	0.235

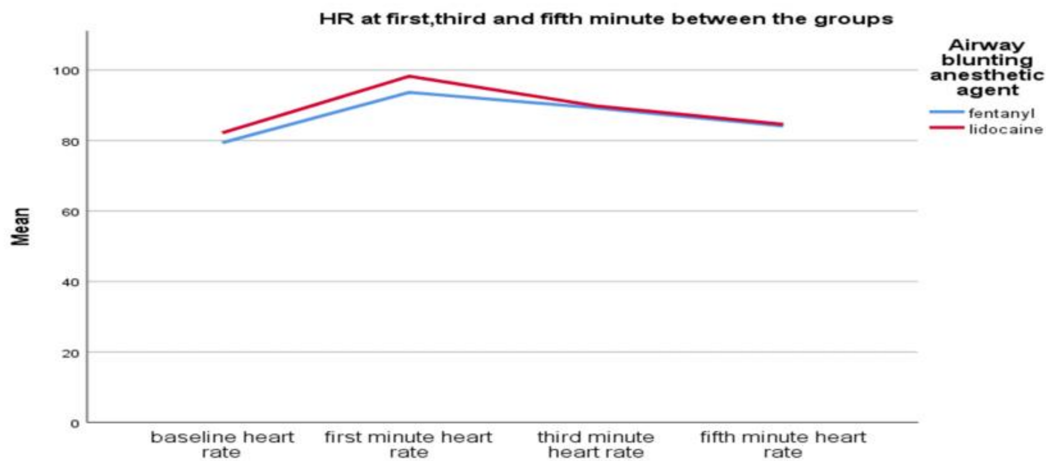
6.3 Comparison of change in HR from base line between groups

The mean change in the HR at the first minute, third minute and fifth minute was not statistically significant between the fentanyl and lidocaine group (their p values are all >0.05). Meaning, the two groups doesn't have a great difference between them in blunting the tachycardia response to direct larytngoscopy and intubation. The p value of the first minute HR between the two groups is 0.064. Even though it doesn't show significance, fentanyl showed a better lesser rise in HR than lidocaine with mean and SD of (93.65+12.32) compared to lidocaine (98.23+10.19) only during first minute.

Table 3. The mean and SD values among the two groups across different time frames

	fentanyl	lidocaine	P value
Baseline HR	79.37±10.42	82.16±9.409	0.196
First minute HR	93.65+12.32	98.23+10.19	0.064
Third minute HR	89.23+13.662	89.79+10.899	0.835
Fifth minute HR	84.09+12.535	84.60+10.709	0.839

Figure 2. Mean HR between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute



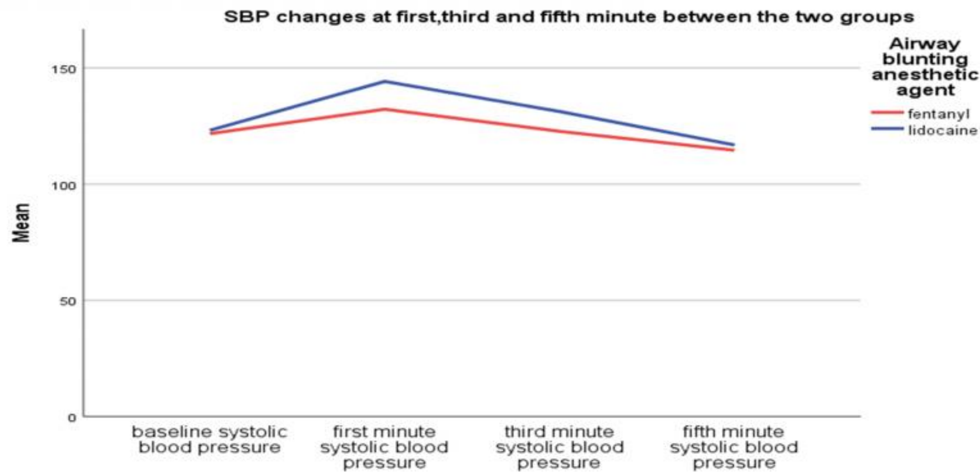
6.3 Comparison of change in SBP from base line between fentanyl and lidocaine

The mean SBP during the first minute after intubation is significantly different between fentanyl (132.21+14.527) and lidocaine(144.16+16.182) with a t value = 3.605, p value=0.001. the third minute SBP is also indicating a difference with fentanyl(122.67+13.305) and lidocaine(131.21+13.981) with a t value=2.9 and p value=0.005. The fifth minute has no significant difference with a p value of >0.05.

Table 4. The mean and SD values of SBP among the two groups across different time frames

	fentanyl	Lidocaine	P value
Baseline SBP	121.67+10.327	123.14+12.338	0.552
First minute SBP	132.21+14.527	144.16+16.182	0.001
Third minute SBP	122.67+13.305	131.21+13.981	0.005
Fifth minute SBP	114.53+11.542	116.81+ 9.818	0.327

*F*igure 3. Mean SBP between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute



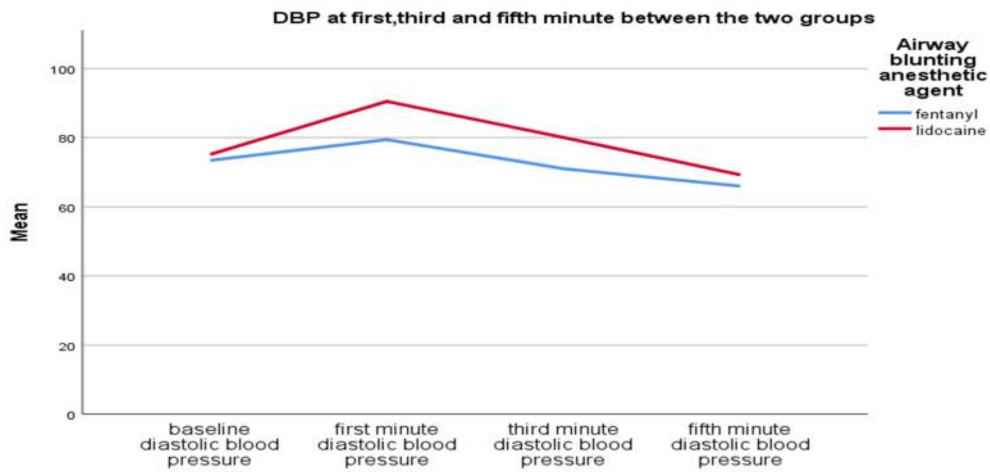
6.4 Comparison of change in DBP after intubation from base line between lidocaine and fentanyl

The mean DBP during first and third minute after intubation is significant with a p value of 0.000, t value=4.17 and p=0.001, t value=3.54 respectively. The first minute p value is zero indicating the two groups of intervention have a great difference regarding DBP change during laryngoscopy and intubation. The fifth minute DBP has no significance between them with p value of > 0.05.

Table 5. The mean and SD of the DBP values among the two groups across different time frames

	fentanyl	lidocaine	P value
Baseline DBP	73.42+13.772	75.16+12.329	0.538
First minute DBP	79.44+11.279	90.49+13.211	0.000
Third minute DBP	71.00+10.852	80.05+12.747	0.001
Fifth minute DBP	65.98+9.701	69.23+8.147	0.096

Figure 4 Mean DBP between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute



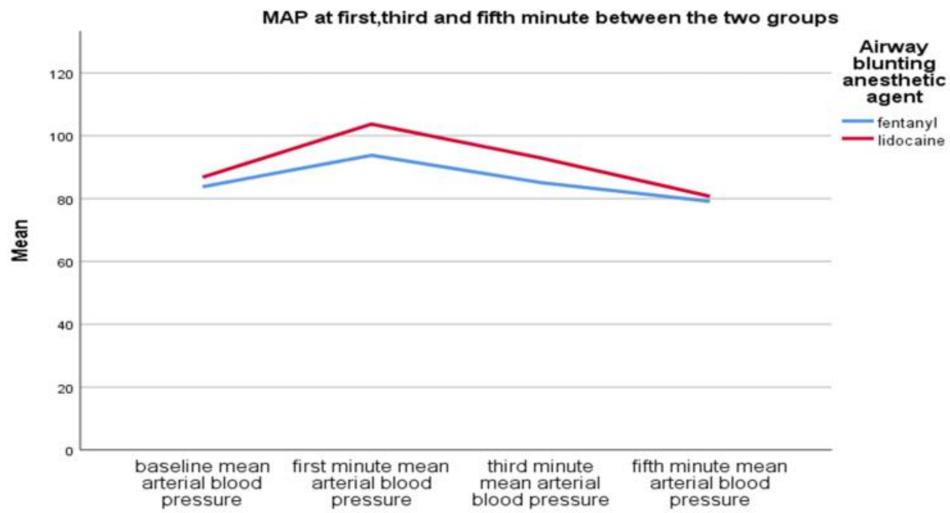
6.5 Comparison of change in mean arterial blood pressure from base line

The mean MAP at first minute for fentanyl (79.44+11.279) and lidocaine (90.49+13.211) has p value of 0.003 and t value of 3.02. The third minute also has p value of 0.006 and t value of 2.8. Both first and third minute values show significant difference between the two groups. The fifth minute MAP has no significant difference with a p value of >0.05.

Table 6. The mean and SD of the MAP values among the two groups across different time frame

	fentanyl	Lidocaine	P value
Baseline MAP	83.77+9.486	86.79+13.611	0.235
First minute MAP	79.44+11.279	90.49+13.211	0.003
Third minute MAP	85.09+9.618	92.93+15.632	0.006
Fifth minute MAP	79.12+9.108	80.70+10.322	0.453

Figure 5. Mean MAP between fentanyl and lidocaine at baseline, 1st, 3rd, 5th minute



7. Discussion

Numerous studies have been conducted comparing the effects of fentanyl and lidocaine on the blunting hemodynamic response to endotracheal intubation and direct laryngoscopy. These studies included either both agents or one of them in regard to another airway blunting agent. Our study focuses on the two drugs specifically to attenuate the tachycardic and hypertensive response of the larygoscopic intubation procedure on elective surgical patients.

Patients suffering from coronary artery disease, cerebrovascular disorders, or hypertension are at grave risk due to the procedure of intubation leading to the development of arrhythmia, myocardial ischemia, infarction, and cerebral hemorrhage(6). Our study tries to compare the commonest agents and the most available ones used for attenuating cardiovascular response.

In this study the use of either fentanyl or lidocaine has a similar effect on the heart rate changes compare to the baseline values on all the recorded timeframes with a P value of >0.05. The peculiar result was during the first minute which had a p value of 0.064, though it doesn't show significance, fentanyl was better than lidocaine in blunting the airway response to intubation. However there is much more variation on the blood pressure especially on the first and third minute. Fentanyl has less SBP, DBP and MAP values compared to lidocaine at the first and third minute with a P value of <0.05. The fifth minute blood pressure changes were similar between the two agents with a P value of >0.05. These indicate both fentanyl and lidocaine has no significant difference in preventing the tachycardia response: though fentanyl has a better capacity at first minute than lidocaine. Additionally fentanyl is much more superior to lidocaine in minimizing the hypertensive response on the initial minutes of the procedure than lidocaine.

Mashhad University of Medical Sciences in Iran did compare fentanyl and lidocaine to blunt pressor response and found that lidocaine blunt both heart rate and mean arterial pressure more than fentanyl. However both do prevent these changes. Compared to our study it has similarity in regard to the heart rate result. However they only studied MAP from the blood pressure parameters; and this variation from our study could be due to their use of etomidate as sedative agent or the variation of the demographics characteristics of the patients. There are patients with comorbidities including cardiac disease and patients with respiratory distress, they included older population unlike ours and the participants were emergency patients (15).

Salman and his colleagues (2019) did a study in basrah comparing the two drugs: they found that both agents were similar regarding their effect on HR and BP even though their blunting capacity of the HR isn't efficient. This conclusion has some similarity with our results especially their effect on the heart rate. However the BP effect is different from ours which states that fentanyl and lidocaine have similar effect. In our study fentanyl is superior to lidocaine in blunting the hypertensive response of the procedure. The variation of result might be due to the difference in the size of the participants in their study which only included 20 participants per group (16).

In dilla university hospital, they studied fentanyl and lidocaine effect on hemodynamic response to intubation. Fentanyl is superior to lidocaine in both HR and BP parameters in the first minute. After the first minute there is no significant difference between them. Our research is similar in regard to their effect on BP only. Dr Anagha(2021) in india compared fentanyl, lidocaine and esmolol in blunting the airway during intubation and finds out fentanyl has more pronounced reduction of BP than the other drugs which is similar with our result(22). The study is more reliable since it used larger sample size for the trial.

There are multiple research which indicate that fentanyl is superior that lidocaine in blunting the hemodynamic response to intubation. Nurul and et al compared fentanyl and lidocaine during intubation. They didn't use a control group like our study and they used 30 participants per group. Their analysis found that fentanyl has less changes in the four hemodynamic parameters compared to lidocaine during laryngoscopic intubation (23). This study resembles our study in major areas and in their conclusion prefers fentanyl for attenuation of airway response during intubation.

8. Strength and limitation

Strength : Some of the strengths include avoiding the possible confounding factors from previous research done in Ethiopia such as; limiting laryngoscopy time, making induction drug choices and maintenance agents constant.

Limitation: The limitations are being single blind study, Lacking control group and lacking protocol to use during during perioperative period.

9. Conclusion and recommendation

9.1 conclusion

Fentanyl has a greater blunting effect than lidocaine, particularly when it comes to the hypertensive response during the first and third minutes of direct laryngoscopy and intubation. Even though the result doesn't indicate significance, the HR response is better attenuated with fentanyl compared to lidocaine.

9.2 recommendation

This study adds to the body of knowledge on the topic of attenuating hemodynamic airway response to direct laryngoscopic intubation, as there aren't many studies of this type. Our study findings indicates that the use of fentanyl with a dose of 2 μg/kg is recommended 3 minutes prior to intubation in order to mitigate the increase in the HR and BP associated with laryngoscopy and intubation. And availing the drug fentanyl in all the OR pharmacy of Ethiopia is our final message. Additionally we recommend the study of additional blunting agent such as esmolol in the future researches.

Reference

1. Hung O, Murphy MF. Hung's difficult and failed airway management. (No Title). 2018.
2. Joffe AM, Deem S. Physiologic and pathophysiologic responses to intubation. Anesthesiology Clinics of North America. 1995;13:361-75.
3. Stoelting RK. Blood pressure and heart rate changes during short-duration laryngoscopy for tracheal intubation: influence of viscous or intravenous lidocaine. Anesthesia & Analgesia. 1978;57(2):197-9.
4. Mahajan L, Kaur M, Gupta R, Aujla KS, Singh A, Kaur A. Attenuation of the pressor responses to laryngoscopy and endotracheal intubation with intravenous dexmedetomidine versus magnesium sulphate under bispectral index-controlled anaesthesia: A placebo-controlled prospective randomised trial. Indian Journal of Anaesthesia. 2018;62(5):337-43.
5. Collins VJ. Principles of anesthesiology: general and regional anesthesia: Lea & Febiger; 1993.
6. Thippeswamy RR, Shetty SR. Intravenous low dose fentanyl versus lignocaine in attenuating the hemodynamic responses during endotracheal intubation: a randomized double-blind study. Anesthesia, essays and researches. 2018;12(4):778.
7. Kumar A, Seth A, Prakash S, Deganwa M, Gogia AR. Attenuation of the hemodynamic response to laryngoscopy and tracheal intubation with fentanyl, lignocaine nebulization, and a combination of both: A randomized controlled trial. Anesthesia, essays and researches. 2016;10(3):661.
8. King B, Harris L, Greifenstein F, Elder J, Dripps R. Reflex circulatory responses to direct laryngoscopy and tracheal intubation performed during general anesthesia. The Journal of the American Society of Anesthesiologists. 1951;12(5):556-66.
9. Kayhan Z, Aldemir D, Mutlu HS, Ö ü E. Which is responsible for the haemodynamic response due to laryngoscopy and endotracheal intubation? Catecholamines, vasopressin or angiotensin? European Journal of Anaesthesiology. 2005;22:780–5.
10. Abou-Madi M, Keszler H, Yacoub O. A method for prevention of cardiovascular reactions to laryngoscopy and intubation. Canadian Anaesthetists’ Society Journal. 1975;22:316-29.

11. Ebert JP, Pearson JD, Gelman S, Harris C, Bradley EL. Circulatory responses to laryngoscopy: the comparative effects of placebo, fentanyl and esmolol. Canadian Journal of Anaesthesia. 1989;36:301-6.

12. STOELTING RK. Circulatory response to laryngoscopy and tracheal intubation with or without prior oropharyngeal viscous lidocaine. Anesthesia & Analgesia. 1977;56(5):618-21.

13. Martin DE, Rosenberg H, Aukburg SJ, Bartkowski RR, Edwards Jr MW, Greenhow DE, et al. Low-dose fentanyl blunts circulatory responses to tracheal intubation. Anesthesia & Analgesia. 1982;61(8):680-4.

14. Feng C-K, Chan K-H, Liu K-N, Or C-H, Lee T-Y. A comparison of lidocaine, fentanyl, and esmolol for attenuation of cardiovascular response to laryngoscopy and tracheal intubation. Acta Anaesthesiologica Sinica. 1996;34(2):61-7.

15. Hashemian AM, Doloo HZM, Saadatfar M, Moallem R, Moradifar M, Faramarzi R, et al. Effects of intravenous administration of fentanyl and lidocaine on hemodynamic responses following endotracheal intubation. The American journal of emergency medicine. 2018;36(2):197-201.

16. Salman J. Comparative study of the efficacy of lignocaine and fentanyl after propofol induction in attenuation of hemodynamic changes following laryngoscopy and endotracheal intubation during general anesthesia. Basrah Journal of Surgery. 2019;25(2):13-20.

17. Doba DN, Ferede ZA, Kasa SM, Gebre EE, Ayalew N, Workneh SA, et al. Comparison of intravenous fentanyl versus lidocaine for attenuation of hemodynamic response to laryngoscopy and endotracheal intubation in patients undergoing elective surgery in Dilla University Referral Hospital, Ethiopia, a randomized controlled trial. IJS Global Health. 2020;3(6):e27.

18. Samuel H, Melekamayhu A, Woldeyohannes M, Tesfaye S, Shitemaw T. A comparative study between intravenous fentanyl and intravenous lidocaine on attenuation of hemodynamic pressor responses to laryngoscopic intubation: a prospective cohort study, Ethiopia. Open Journal of Anesthesiology. 2019;9(9):167-78.

19. Wondimu S, Bekele S, Giorgis DG, Getachew F, Seyoum N. Pattern of surgical admissions to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A five-year retrospective study. East and Central African Journal of Surgery. 2018;23(2):66-70.

20. Khan AA, Khan FA. Haemodynamic response to induction, laryngoscopy and tracheal intubation in diabetic and non-diabetic patients. Journal of the Pakistan Medical Association. 2009;59(1):27.

21. Anagha Joy, Hema Vadakkoot Raghavan, Bindu M, Sunil M, Randeep A.M. A Comparative Study on the Effects of Intravenous Esmolol, Fentanyl And Lignocaine On Attenuation Of Hemodynamic Response To Laryngoscopy And Endotracheal Intubation, journal of clinical pharmacology.2024,

22 Islam, N., Mondal, S. K., Begum, M., Begum, R., Hossain, M., Mohammad, T., & Alam, S. S. Role of intravenous fentanyl and lignocaine for attenuation of stress response in endotracheal intubation Journal of the Bangladesh Society of Anaesthesiologists,(2017) 30(2), 96–101.

Annex

Annex 1: Questioner

Instruction: For each of the questions, please circle the number of alternative(s) that fit the response, fill the blank space provided or provide appropriate response accordingly.

Part I

Questions on socio demographic characteristics of the patients		
1	Age(years)	
2	Sex	A. F B. M
3	weight	
4	ASA Class	A. ASA 1 B. ASA 2

Part II

Questions regarding surgical and anesthetic information		
1	Mallapati grading	A. 1 B. 2
2	Surgical procedure type	A. Gastrointestinal B. Chest C. Vascular D. Gynecologic E. ENT F. Urologic G. Orthopedic H. Others…
3	The anesthetic agent used 3 minute prior to intubation	A. Fentanyl B. Lidocaine

PART III

Information on Hemodynamic parameters				
Hemodynamic parameters	Heart rate (HR)	Systolic blood pressure(SBP)	Diastolic blood pressure(DBP)	Mean arterial pressure(MAP)

Baseline(before intubation)				
1st minute after intubation				
3rd minute after intubation				
5th minute after intubation				

Part 4 IV

MAC immediately used after induction		
1	Isoflurane	A. 1% B. 1.5% C. 2% D .Specify….

Annex 2: Subject information sheet

Addis Ababa University

School of medicine

Subject information sheet

Hello, my name is --------------------------------, I am here in behalf of Dr. Mezmure Kenea, a student in Addis Ababa University School of medicine. She is conducting a research on "Comparative Study between Intravenous Lidocaine and Fentanyl in Attenuating Cardiovascular Response To laryngoscopic Intubation in Adult Patients Undergoing Elective Surgery in TASH in 2023, Addis Ababa, Ethiopia". She has received permission from Addis Ababa University School of medicine and Tikur Anbessa Specialized Hospital officials to conduct the study.

You were selected to participate in this study because you are currently working as an anesthesia provider at TASH. Your participation in this study will only be based on your willingness to participate. You have the right to choose not to take part in this study. If you are willing, you have the right to stop at any time or withdraw without giving any reason, and you will not be subjected to any ill-treatment. There will be no direct benefit from participating in this study, but in the future, the information gathered by this study will help improve the quality of the care that will be given not only in TASH but also in other institutions.

The information that you provide will be kept confidential by using only code numbers and locking the data. Only the members of the study team will have the access to the non-coded data and the data will not be used for purposes other than the study. Your willingness and active participation is very important for the success of this study.

If you need any further information or explanation regarding to the study, you can have this address to contact.

Name: Dr. Mezmure Kenea   Tel- +251-940197263

Email- mezmurekenea1995@gmail.com

Annex 3: informed consent form

አመሰግናለሁ፡፡

ስሜ መዝሙረ ቀነአ እባላለሁ፡፡

እኔ በአዲስ አበባ ዩኒቨርሲቲ በአንስቴዥዮሎጂ ት/ት ክፍል ተማሪ ስሆን የመመረቅያ ፅሁፌን በቀዶ ህክምና ወቅት የአየር ቧንቧን ለመቆጣጠር በጉሮሮ ዉስጥ በሚገባ ቱቦ ምክንያት የሚከሰቱ ችግሮችን ለመቅረፍ ለህመሙማን በሚሰጡ መድሀኒቶች ዙርያ አደርጋለው፡፡ ከዚሁ ጥናት የሚገኘዉ መረጃ የጤና ባለሙያዎችን በጥሩ ሁኔታ ታካሚዎችን እንዲረዱ ያግዛቸዋል፡፡ በመሆኑም የርስዎ በጥናት ዉስጥ መካትተ ለዚህ ጥናት መሳካት ከፍተኛ አስተዋጾ አለዉ፡፡ ከርስዎ እና ከ ሕክምና ካርዶዎ በ ተጨማሪ በየሕክምና ወቅት የምናገኘዉን ማንኛዉም መረጃ እና ምርምር አገልግሎት ላይ እንደምናዉል እየገለጽኩኝ በማንኛዉም ሁኔታ የርስዎ የግል መረጃ ለሌላ አገልግሎት እንደማይዉል ለማሳሰብ እወዳለሁ፡፡

እንድንቀጠል ይፈቅዳሉ ? አዎ--------------- አልፈልግም--------------

(ስለ ዕርዳታዎ በቅድሚያ ላቅ ያለ ምስጋና አቀርባለሁ፡፡)

የ አጥኚዋ ስም ና አድራሻ

ዶ/ር መዝሙረ ቀነአ : mezmurekenea1995@gmail.com

ስልክቁጥር : (+251) 940197263