# ADDIS ABABA UNIVERSITY
# COLLEGE OF HEALTH SCIENCES
# SCHOOL OF MEDICINE
# DEPARTMENT OF ANESTHESIA


EFFECTIVENESS OF INTRAVENEOUS LIDOCAINE AND FENTANYL ON ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION FOR EAR, NOSE AND THROAT SURGERIES IN YEKATIT 12 HOSPITAL MEDICAL COLLEGE, ADDIS ABABA, ETHIOPIA 2018.

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# ABSTRACT

**Background:** Tracheal extubation, the purposeful removal of the endotracheal tube from the trachea, can be associated with detrimental hemodynamic and airway responses. Lidocaine and fentanyl are known to suppress hemodynamic response to extubation during Ear, nose, and throat surgeries. Smooth tracheal extubation is important after Ear, nose, and throat surgeries.

**Objective:** To compare the effect of intravenous lidocaine and fentanyl on attenuation of hemodynamic response to extubation for Ear, nose, and throat (ENT) surgeries at Yekatit 12 Hospital Medical College.

**Methods:** This prospective cohort study recruits 74 American Society of Anesthesiologist (ASA) class I and II, age between 18 and 60 patients who underwent Ear, Nose and Throat surgeries. Unpaired T test was used to compare the mean of heart rate and mean arterial blood pressure between groups. Mann Whitney U Test was used for distribution free data. Association of categorical independent variables between two groups were analyzed using Chi Square or fisher exact test. P-values < 0.05 were considered as statistically significant with a power of 80%.

**Results:** The demographic and clinical characteristics were comparable between groups. The pulse rate and mean arterial blood pressure were significantly lower in fentanyl group at 1, 5, and 10 min after extubation with p values < 0.05. There was no statistically significant difference between two groups with decreasing the incidence of coughing in the Periextubation period with a p value of 0.857.

**Conclusion and Recommendation:** The findings of our study demonstrate that fentanyl 1µg/kg IV, administered 10 min before end of operation, was more effective in attenuating hemodynamic response to tracheal extubation compared with lidocaine 1.5 mg/kg IV in patients underwent ENT surgeries. We recommend that fentanyl administered 10 minutes before the end of operation for ENT surgeries is effective in attenuating hemodynamic response to extubation.

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# List of Abbreviations

ASA-American Society of Anesthesiology

BMI – Body Mass Index

BP – Blood Pressure

ENT – Ear, Nose, Throat

ETTI – Endotracheal Tube Intubation

GA – General Anesthesia

HR - Heart Rate

IV - Intravenous

Kg - Kilo gram

MAP – Mean Arterial Blood Pressure

Min – Minute

ml - milliliter

mmHg – millimeter mercury

RCT - Randomized Controlled Trial

Y12HMC – Yekatit 12 Hospital Medical College

# 1. INTRODUCTION

## 1.1 Background

Tracheal extubation can be associated with detrimental hemodynamic and airway responses. Smooth extubation requires the absence of straining, coughing, breath holding and laryngospasm (1).

Deep extubation refers to the removal of a tracheal tube in a spontaneously breathing patient who is sufficiently anesthetized to obtund the laryngeal reflexes. This technique offers the advantage of a smooth extubation with less airway stimulation, thereby reducing cardiovascular stimulation, coughing, intraocular, intracranial, and middle ear pressure changes. However, the risks of deep tracheal extubation include increased incidence of airway obstruction and aspiration (2).

In order to control hemodynamic changes during tracheal intubation and extubation, local anaesthetics, opioids, beta-blocking agents, and calcium channel blockers have been used with varying success rates (3).

Fentanyl, an opioid agonist, may blunt cardiovascular and airway reflexes during emergence without prolonging the recovery. It predominantly acts on μ receptors. Fentanyl brings hemodynamic stability during perioperative period by its action on cardiovascular and autonomic regulatory areas. It decreases sympathetic tone and increases parasympathetic tone. Fentanyl inhibits pituitary adrenal response directly or indirectly via hypothalamus. Low dose (1 microgram/ kilogram) of fentanyl was employed because a large dose may lead to muscular rigidity, bradycardia, nausea and vomiting. Large doses may also cause postoperative respiratory depression (4).

Lidocaine attenuates the hemodynamic response to tracheal extubation by its direct myocardial depressant effect, central stimulant effect, and peripheral vasodilatory effect and finally it suppresses the cardiovascular and airway reflexes, an effect on synaptic transmission (5). So we had considered lidocaine in our study.

## 1.2 Statements of the problem

Stimulation of various sites, from the nasal mucosa to the diaphragm can increase hemodynamic and airway reflexes (6). Stable hemodynamics during emergence and smooth emergence are especially important in patients undergoing oral surgery, because the operative site is an airway structure, and thus, presents risks of bloody aspiration and airway obstruction due to soft tissue edema (7). It is always a challenging task to perform smooth extubation while avoiding coughing, breath holding, oxygen desaturation, and laryngospasm in patients undergoing adenotonsillectomy (8). For patients undergoing otologic surgery, coughing can generate acute increases in pressure transmitted to the middle ear through the eustachian tubes, which may dislodge tympanic membrane grafts or disrupt other repairs (2).

Coughing due to airway irritation during extubation can cause harmful effects such as hypertension, tachycardia, arrhythmia, myocardial ischemia, bronchospasm, bleeding at operative site, intracranial and intraocular hypertension (9).

To reduce hemodynamic and airway reflexes, tracheal extubation should be performed while the patient is deeply anesthetized or with drugs that do not depress ventilation (6). Extubation under deep anaesthesia decreases cardiovascular stimulation and reduces the incidence of coughing and straining on the tube. However, the incidence of respiratory complications has been found to be greater after extubation under deep anaesthesia, regardless of the type of operation. The incidence of complications dramatically decreased when extubation was performed when eyes were open, with spontaneous ventilation. (10).

Many drugs have been advocated to minimize these hemodynamic and airway adverse responses during extubation such as: fentanyl(11,12), remifentanil(13), sufentanil(14), esmolol(15,16), dexmedetomidine(17,18), lidocaine(4,19), propofol(20,21).

There are some studies in different foreign countries on minimizing hemodynamic response to laryngoscopy and intubation but little emphasis has been given to endotracheal extubation. Fentanyl, an opioid agonist, may blunt cardiovascular and airway reflexes during emergence without prolonging the recovery (22).

Hence, the aim of this study was to compare the effect of intravenous lidocaine and fentanyl on attenuation of hemodynamic response to extubation for ENT surgeries.

## 1.3 Significance of the study

Endotracheal extubation is an unpredictable and tricky part of anaesthetic management. Elevation in blood pressure and heart rate due to extubation are transient but may have significant effects.

Recommendations are manifold but the technique, besides minimizing the cardiovascular responses to extubation must also satisfy the following requirements. It must be applicable universally and easily, neither be time consuming nor affect the duration of anaesthesia(21). Among the recommended procedures intravenous lidocaine & fentanyl fulfil the above criteria.

Even if it is not enough some studies conducted in Asia showed that hemodynamic and airway response to extubation can be attenuated by lidocaine and fentanyl. Some literatures shows conflicting results on effectiveness of lidocaine and fentanyl for attenuating hemodynamic responses to extubation.

The reason why we will do our research is that, it generates information that may help program planners to develop effective preventive strategies, to select the best alternative solution and to evaluate effectiveness of implemented preventive intervention targeted to the problem.

As far as my knowledge goes there is no published research conducted in our country so that it can be used as a base line data for further research

# 2. LITERATURE REVIEW

Securing airway with endotracheal intubation forms the mainstay of standard general anesthetic practice. Similar to intubation, extubation is also associated with various circulatory and airway responses due to reflex sympathetic activity following stimulation of epipharyngeal and laryngo-pharyngeal structures. Following extubation respiratory complications have been three times more common than those occurring during intubation (4.6% versus 12.6%)(22).

Even if it is not enough some studies showed that hemodynamic and airway response to extubation can be attenuated by lidocaine and fentanyl. But there were studies that shows conflicting results on effectiveness of lidocaine and fentanyl for attenuating hemodynamic responses to extubation.

A 2009 Turkey RCT study did not show the effectiveness of fentanyl in attenuating hemodynamic response to extubation. There were no clinically significant decreases in HR and in BP after extubation with fentanyl. In the fentanyl group, HR was significantly increased compared with the preextubation values (P = 0.007). SBP was significantly increased at 1, 5, and 10 minutes after extubation in the fentanyl group (P = 0.033). Fentanyl was also associated with a significant decrease in extubation quality, reflected in the prevalence of coughing after extubation in 85% of patients (6).

An Indian RCT study also did not show the effectiveness of fentanyl in attenuating hemodynamic response to extubation. Ten minutes prior to extubation Fentanyl 1µg /kg was infused over 10 minutes period. Hemodynamic parameters were noted at extubation, 2, 4, 6, 8, 10 min after extubation. All the measured hemodynamic parameters were significantly elevated at extubation and at various points of observation in fentanyl group. Fentanyl group had lower score of extubation quality, which shows smooth extubation (22).

A 2016 Indian study done on rapid and reliable smooth extubation, was comparing fentanyl 1 µg/kg with dexmedetomidine 0.75 µg/kg. There was stastisticaly significant drop in blood pressure at 5 min after test drug administration in the fentanyl group (1).

Another study conducted on hemodynamic response to extubation which compares Lidocaine, Esmolol and Propofol given two minutes prior to extubation. This study shows the efficacy of lidocaine on attenuating cough to extubation. Lidocaine able to attenuate cough in > 90% of the patients(21).

A 2011 Korean study conducted in patients who were divided into control group and 1.5 mg/kg of lidocaine spray, sprayed onto laryngeal and intratracheal sites (10% lidocaine group) 2 min prior to intubation. MAP at 2.5 and 5 min ($P < 0.05$) and HR at 2.5 min after laryngoscopy ($P < 0.01$) were greater in the control group than in the 10% lidocaine group. The number of coughs decreased in 10% lidocaine group compared to the control group during pre- and post-extubation period of 5 min and during the entire study period ($P < 0.001$) (9).

A 2014 Japan systematic review and meta-analysis on the effects of intravenous and/or topical lidocaine on the incidence of laryngospasm during general anaesthesia which includes 9 randomized controlled trials including 787 patients were analysed. The combined results demonstrated that lidocaine is effective in preventing laryngospasm (risk ratio (RR) 0.39, 95% CI 0.24–0.66; I2 = 0). Subgroup analysis revealed that both intravenous lidocaine (RR 0.34, 95% CI 0.14–0.82) and topical lidocaine (RR 0.42, 95% CI 0.22–0.80) in preventing laryngospasm. Both topical and intravenous lidocaine are effective for preventing laryngospasm (23).

A study conducted in Iran in 2011 comparing lidocaine 1.5mg/ kg either intravenously or intratracheally. There was no significant difference in the number of coughs during the 30-min monitoring after extubation between two groups with p value of 0.97 (24).

A study done in India in 2012**,** comparing fentanyl 4 micrograms/kg and lidocaine 1.5mg/kg and then third group received placebo (normal saline). After intubation incidence of tachycardia (HR>100/ min) was significantly greater in placebo and lignocaine group than in fentanyl group ($p<0.05$). Rise in SBP and DBP were also statistically significant in lidocaine group than in fentanyl group ($p<0.05$) (4).

Another 2015 Indian RCT study with controlled hypertension patients randomly divided into fentanyl group received 2 mcg/kg and the fentanyl plus lidocaine group received 1.5mg/kg lidocaine and fentanyl 2mcg/kg, 3 min prior to intubation. There were no significant differences

between the two groups regarding hemodynamic parameters like heart rate, systolic blood pressure and diastolic blood pressure (11).

A 2011 Iran study on patients with hypertension were divided into two groups (fentanyl group and fentanyl plus lidocaine group). The fentanyl group received 2 mcg/kg and the fentanyl plus lidocaine group received 1.5mg lidocaine and 2mcg/kg fentanyl. There were no significant differences between the two groups regarding heart rate, systolic blood pressure and diastolic blood pressure (12).

A 2011 Nigerian study, comparing 2% lidocaine jelly (LJ) or K-Y jelly (KYJ) for the groups and the patients were interviewed at 1, 12 and 24 hours post extubation. The incidence cough were decreased in the LJ group (25).

# 3. OBJECTIVE OF THE STUDY

## 3.1 General objective

To compare the effects of intravenous lidocaine and fentanyl on attenuation of hemodynamic response to extubation for patients undergoing ENT surgeries in Yekatit 12 Hospital Medical College from January 01, 2018 to March 30, 2018.

## 3.2 Specific objectives

To compare the effect of lidocaine and fentanyl on heart rate to extubation.

To compare the effect of lidocaine and fentanyl on blood pressure to extubation.

To compare the effect of lidocaine and fentanyl on quality of extubation.

# 4. METHODOLOGY

## 4.1 Study Area and period

This study was conducted at Yekatit 12 Hospital Medical College which is located in the capital city of Ethiopia, which is one of the governmental hospitals in Addis Ababa, The hospital was named after, Yekatit 12 is a date in the Ethiopian calendar, which is used to refer to the indiscriminate massacre, known as the Addis Ababa massacre, and imprisonment of Ethiopians by elements of the Italian occupation forces following an attempted assassination of Marshal Rodolfo Graziani, Marchese di Neghelli, Viceroy of Italian East Africa, on 19 February 1937. The hospital gives service for different unties like; medical, surgical, pediatrics wards, ICU, operation room and recovery room. Y12HMC have one obstetric, two burn, one ENT, one maxillofacial and four surgery operation theaters. There are also 2 Post Anesthesia Care Units which have 6 beds for ENT, maxillofacial and general surgery. The study was conducted from January 1 to March 30, 2018.

## 4.2 Study design

Institutional based prospective cohort study design was employed.

## 4.3 Population

### 4.3.1 Source Population

All adult patients who were scheduled for elective ENT surgeries under GA with ETTI at Yekatit 12 Hospital Medical College.

### 4.3.2 Study Population

All adult patients who underwent elective ENT surgeries under GA with ETTI at Yekatit 12 Hospital Medical College during the study period.

## 4.4 Study variable

### 4.4.1. Dependent Variables

-Heart rate

-Mean arterial blood pressure

-Quality of extubation

### 4.4.2 Independent Variables

-Age

-Sex

-ASA

-BMI

-Type of procedure

-Type of induction agent

-Anesthetist experience

-Surgeon experience

- Estimated blood loss

- Duration of surgery

- Duration of anesthesia

Exposure variable; Lidocaine or Fentanyl

## 4.5 Operational definitions

**Tachycardia and bradycardia response** in our study was defined as increase and decrease in heart rate ≥ 30 beats per minute from baseline value respectively.

**Hypertensive and hypotensive response** was defined as increase and decrease in mean arterial blood pressure ≥ 30 mmHg from baseline value respectively.

These responses are adopted from (22).

**Baseline value:** Hemodynamic measured prior to the study drug administration and before extubation was defined as baseline value.

**Extubation quality scale**

No coughing

Minimal coughing (1 or 2 times)

Moderate coughing (3 or 4 times)

Severe coughing (5-10 times)

Poor extubation (laryngospasm and coughing >10 times)

This scale is adopted from(22).

**Periextubation period:** in our study was defined as period from 10 minutes before the end of operation to first 15 minutes after extubation.

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

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

**ASA status**: is a surgical risk stratifications validated by American Society of Anesthesiologist; described as follows:

**ASA I**: a healthy patient with no organic/physiological/pyschtric problems

**ASA II:** controlled medical conditions with mild systemic effect and no limitation of functional ability

**ASA III**: medical condition with severe systemic effect, limitation in functional capacity

**ASA IV**: poorly controlled medical conditions associated with significant impairment in functional ability that is potential threat to life

**ASA V**: critical condition, little chance of survival without surgical procedure
**ASA VI**: brain dead patient undergoing organ donation

## 4.6 Inclusion and Exclusion criteria

### 4.6.1 Inclusion criteria

-Elective ENT surgeries under GA with ETTI

-ASA status I and II

-Patients age between 18 and 60 (2).

-Patients BMI between 18.5 and 29.5 (6).

### 4.6.2 Exclusion criteria

- Patients with cardiorespiratory abnormalities (Hypertension, New York Heart Association heart failure grades 3 and 4, bronchial asthma, chronic obstructive pulmonary disease, and restrictive lung disease) (22).

- Active upper respiratory tract infection

- Renal dysfunction

- Liver dysfunction.

- History of allergy of the study drugs

-Patients on beta blockers

-Patient refusal

## 4.7 Sampling Technique and Sample Size Determination

### 4.7. 1. Sample size determination

Two independent sample size formula was used to calculate sample size for each group.

$$n = \frac{(S_1^2 + S_2^2)(a + b)^2}{(x_1 - x_2)^2}$$

Where n = the sample size in each of the groups

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

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

X1 - X2 = the mean difference

The means and variances of the two respective groups are $(x1, s1^2)$ and $(x2, s2^2)$. Study shows the diastolic blood pressure changes before and after extubation from intravenous lidocaine group is $7.8 \pm 7$ (mean, SD) and from fentanyl group $13 \pm 8$ (mean, SD) (22),(24).

I have plan to get 80% power of significant result, sample size were n1=37 & n2=37. Adding 10% of non-response rate a total of 74 patients were involved in the study.

### 4.7.2. Sampling technique

Systematic random sampling technique was used till to get the required sample size during the study period. The daily operation schedule list which was used as a sampling frame. The situational analysis show that 13 patient who fulfilled our inclusion criteria is operated in Y12HMC log book per week; according to this data we had 156 patients in our study period from whom we collected data from only 74 patients.

Therefore, K=N/n= 156/74 = 2 (skip interval) and the first participant (random start) was selected using lottery method. Then, every two patients were included in this study from the daily operation schedule list.

## 4.8 Data Collection Technique

Questionnaires were prepared in both in English and Amharic languages which included demographic data and clinical characteristics, hemodynamic parameters and extubation quality. Hemodynamic parameters were recorded before anesthesia, before drug administration (10 min before end of operation), after drug administration (5 min before end of the operation), 1 min, 5 min, 10 min and 15 min after extubation. The data collection was under taken by two MSc and one BSc Anesthetists after getting training and the principal investigator was supervised the completeness of the data daily.

## 4.9 Data Quality Control

Data collectors were trained by principal Investigator.

Pretest was done for 1 week at Y12HMC with 5 % of the total sample size. During data collection, regular supervision and follow up was made.

Principal Investigator was cross checked for completeness and consistency of data every day.

All materials used for data collection was arranged sequentially and data was stored in safe and secured place.

## 4.10 Data Analysis and Interpretation

Data was checked manually for completeness and then coded and entered into Epinfo version 7. Data was cleaned and analysed with SPSS version 20 computer program.

Descriptive statistics, tables and figures were used to summarize data. Shapiro Wilk test were used to test for distributions of data while homogeneity of variance were assessed using Levene's test for equality of variance. Chi square or fisher exact test was used for categorical data. Unpaired t-test and Mann Whitney test were used for comparing numerical variables of normally distributed and skewed data respectively. Data were expressed in terms of mean ± SD for normally distributed data or median (inter quartile range) for skewed data. P-value less than 0.05 was considered as statistically significant with a Power of 80%.

## 4.11 Ethical Consideration

Ethical clearance was obtained from the university ethical clearance committee. The importance of the study were explained & verbal informed consent was obtained from each participant by the data collectors. Confidentiality was maintained at all levels of the study by avoiding identifiers and using codes to identify patients. Participants involvement in the study was on voluntary bases, participants who were not willing to participate in the study and those who wish to quit their participation at any stage was informed to do so without any restriction.

## 4.12 Dissemination plan

Copies of the research will be disseminated to colleges of health science, schools of medicine, department of anesthesia, Addis Ababa University student research office, Ethiopian Association of Anesthetists, Different NGOs, and Ethiopian ministry of health and it can also presented for national and international conferences. Finally it will sent to different national and international journal publishers for publication.

# 5. RESULTS AND DISCUSSION

## 5.1 Results

### 5.1.1 Demographic and clinical Characteristics

Seventy four patients under general anesthesia with endotracheal tube intubated and scheduled for elective ENT surgeries who full filled inclusion criteria were included and completed the study. There was no statistically significant difference between two groups in age. The demographic status and clinical characteristics of data were comparable between groups (table 1).

Table 1: demographic and clinical characteristics of patients who underwent ENT surgeries in Yekatit 12 Hospital Medical College, January 01 to March 30, 2018.

| | Fentanyl group (n=37) | Lidocaine group (n=37) | p- value |
|---|---|---|---|
| Age(years) (mean ± SD) | 26.32 ± 4.52 | 26.41 ± 4.18 | 0.936 |
| Sex<br>Male (n, %)<br>Female (n, %) | <br>24(64.9%)<br>13(35.1%) | <br>21(56.8%)<br>16(43.2%) | <br>0.634 |
| ASA Status<br>ASA 1 (n, %)<br>ASA 2 (n, %) | <br>31(83.8%)<br>6(16.2%) | <br>35(94.6%)<br>2(5.4%) | <br>0.261 |
| BMI ( $Kg/m^2$) (mean ± SD) | 21.34 ± 1.15 | 21.66 ± 1.25 | 0.252 |
| HR before anesthesia (mean ± SD) | 80.35 ± 3.58 | 79.46 ± 4.60 | 0.335 |
| MAP before anesthesia (mean ± SD) | 88.16 ± 4.91 | 87.84 ± 3.63 | 0.747 |
| $SPO_2$ before anesthesia # | 96(96-97) | 97(96-97) | 0.676 |
| Procedure<br>Tonsillectomy (n, %)<br>Tympanoplasty (n, %)<br>Polypectomy (n, %) | <br>20(54.1%)<br>6(16.2%)<br>11(29.7%) | <br>19(51.4%)<br>7(18.9%)<br>11(29.7%) | <br>0.950 |
| Tramadol dose (milligram) # | 60(10) | 60(10) | 0.807 |
| Induction agent<br>Propofol<br>Ketamine & propofol | <br>28(75.7%)<br>9(24.3%) | <br>22(59.5%)<br>15(40.5%) | <br>0.214 |
| Anesthetist experience(years) # | 5(2) | 5(2) | 0.554 |
| Surgeon experience<br>Resident (n, %)<br>Senior (n, %) | <br>8(21.6%)<br>29(78.4%) | <br>11(29.7)<br>26(70.3%) | <br>0.595 |
| Blood loss (milliliter) # | 200(200) | 100(300) | 0.186 |
| Duration of surgery (minute) # | 60(30) | 60(35) | 0.711 |
| Duration of anesthesia (minute) # | 90(40) | 85(43) | 0.736 |

# = Median (Interquartile range); n (%) = number (proportion), SD=Standard deviation

### 5.1.2 Comparison of hemodynamic parameters between Lidocaine and Fentanyl groups

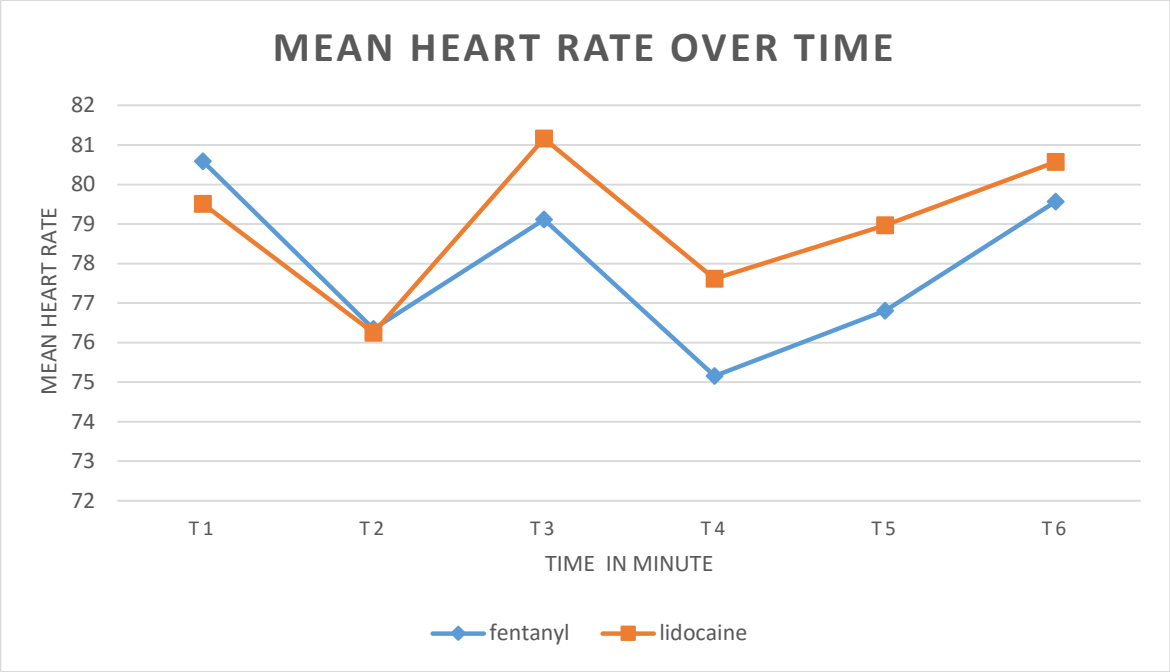
The pulse rate and the mean arterial blood pressure were analysed by unpaired student t test and expressed in mean and standard deviation (mean ± SD). Spontaneous oxygen saturation ($SPO_2$) was analysed by Mann Whitney test and expressed in median and inter quartile range (IQR). The PR and MAP taken before extubation were comparable between two groups except there was a significant difference between two groups in MAP after drug administration (p-value= 0.021).

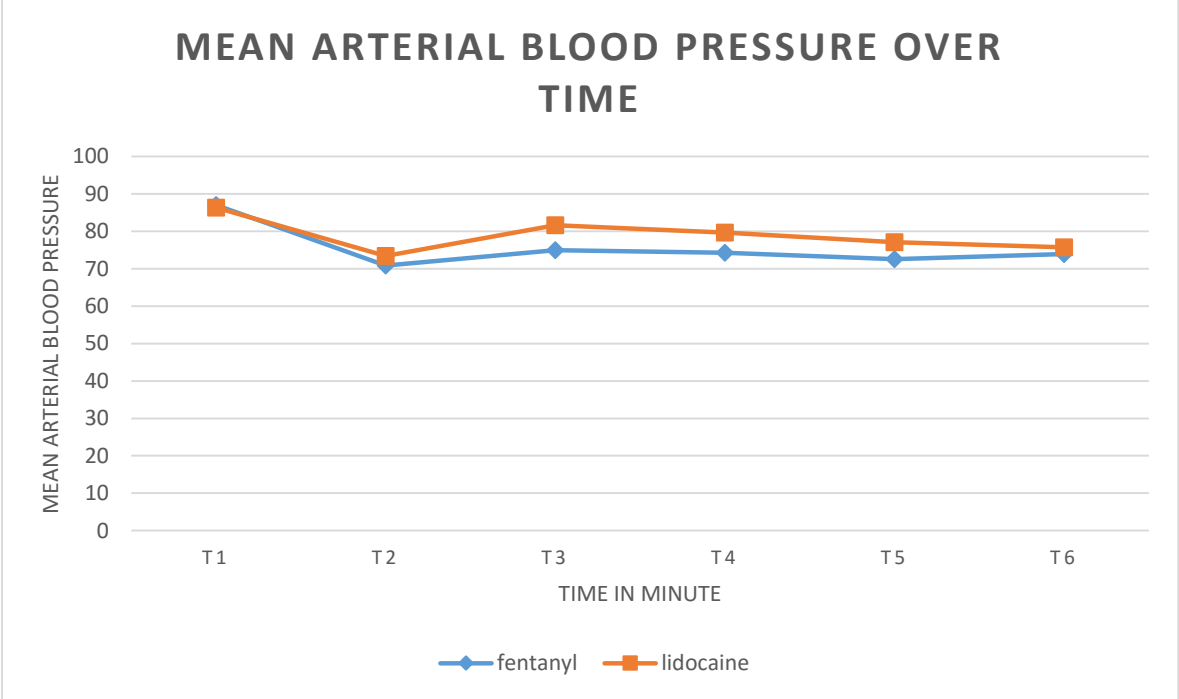
There was a statistically significant difference in PR with mean ± SD in fentanyl group (79.11 ± 3.36) when compared to lidocaine group (81.16 ± 4.24) immediately after extubation with p value of 0.024. There was a statistically significant difference in MAP in fentanyl group (74.97± 3.25) and in lidocaine group (81.65±6.40) at 1 min after extubation (p <0.0001). There were also a statistically significant difference in PR and MAP at 5 and 10 min after extubation (p < 0.05) as shown in Table 2 below.

Table 2: Comparison of hemodynamic parameters for patients underwent ENT surgeries in Yekatit 12 Hospital Medical College, January 01 to March 30, 2018.

| Vital sign | Fentanyl group (n=37) | Lidocaine group (n=37) | p- value |
|---|---|---|---|
| Vital sign before study drug administration | | | |
| PR in bpm (mean ± SD) | 80.59 ± 4.96 | 79.51 ± 4 | 0.306 |
| MAP in mmHg (mean ± SD) | 87.03 ± 4.11 | 86.35 ± 3.96 | 0.474 |
| $SPO_2$ in % # | 100(99-100) | 99(99-100) | 0.109 |
| Vital sign after study drug administration | | | |
| PR in bpm (mean ± SD) | 76.35 ± 5.02 | 76.25 ± 3.25 | 0.935 |
| MAP in mmHg (mean ± SD) | 70.84 ± 3.69 | 73.38 ± 5.40 | 0.021* |
| $SPO_2$ in % # | 100(99-100) | 100(99-100) | 0.714 |
| Vital sign immediately after extubation | | | |
| PR in bpm (mean ± SD) | 79.11 ± 3.36 | 81.16 ± 4.24 | 0.024* |
| MAP in mmHg (mean ± SD) | 74.97 ± 3.25 | 81.65 ± 6.40 | <0.0001* |
| $SPO_2$ in % # | 96(96-97) | 97(96-97) | 0.505 |
| Vital sign 5 min. after extubation | | | |
| PR in bpm (mean ± SD) | 75.16 ± 3.45 | 77.62 ± 3.26 | 0.002* |
| MAP in mmHg (mean ± SD) | 74.27 ± 4.83 | 79.68 ± 5.31 | <0.0001* |
| $SPO_2$ in % # | 97(96-97) | 97(96-98) | 0.229 |
| Vital sign 10 min. after extubation | | | |
| PR in bpm(mean ± SD) | 76.84 ± 3.12 | 78.97 ± 2.57 | 0.002* |
| MAP in mmHg (mean ± SD) | 72.54 ± 4.12 | 77.11 ± 7.44 | 0.002* |
| $SPO_2$ in % # | 97(96-97) | 97(96-97) | 0.844 |
| Vital sign 15 min. after extubation | | | |
| PR in bpm (mean ± SD) | 79.57 ± 4.69 | 80.57 ± 4.63 | 0.359 |
| MAP in mmHg (mean ± SD) | 73.92 ± 4.43 | 75.68 ± 5.79 | 0.147 |
| $SPO_2$ in % # | 97(96-97) | 97(96-97) | 0.565 |

IQR- inter quartile range, SD- standard deviation, PR- pulse rate, MAP- mean arterial blood pressure, *- statistically significant, # = Median (Interquartile range).




T1: Before medication (10 min before the end of operation), T2: After medication (5 min before the end of operation), T3: 1 min after extubation, T4: 5 min after extubation, T5: 10 min after extubation, T6: 15 min after extubation.

Figure 1: Hemodynamic variations over time between fentanyl and lidocaine group patients who underwent ENT surgeries in Yekatit 12 Hospital Medical College, January 01 to March 30, 2018.

### 5.1.3 Comparison on the effect of the Lidocaine and Fentanyl groups on quality of extubation

The association of coughing between groups were analysed by Chi square. The proportions of patients with no coughing were 59.5% in fentanyl group and in lidocaine group which was 64.9%. The proportion of patients with minimal coughing was 27% in fentanyl group and in lidocaine group which is 21.6% and patients with moderate coughing is 13.5% in both groups. Though there was a proportion difference, there was no statistically significant difference between two groups with decreasing the incidence of coughing in the Periextubation period with a p value of 0.857 (figure 2).

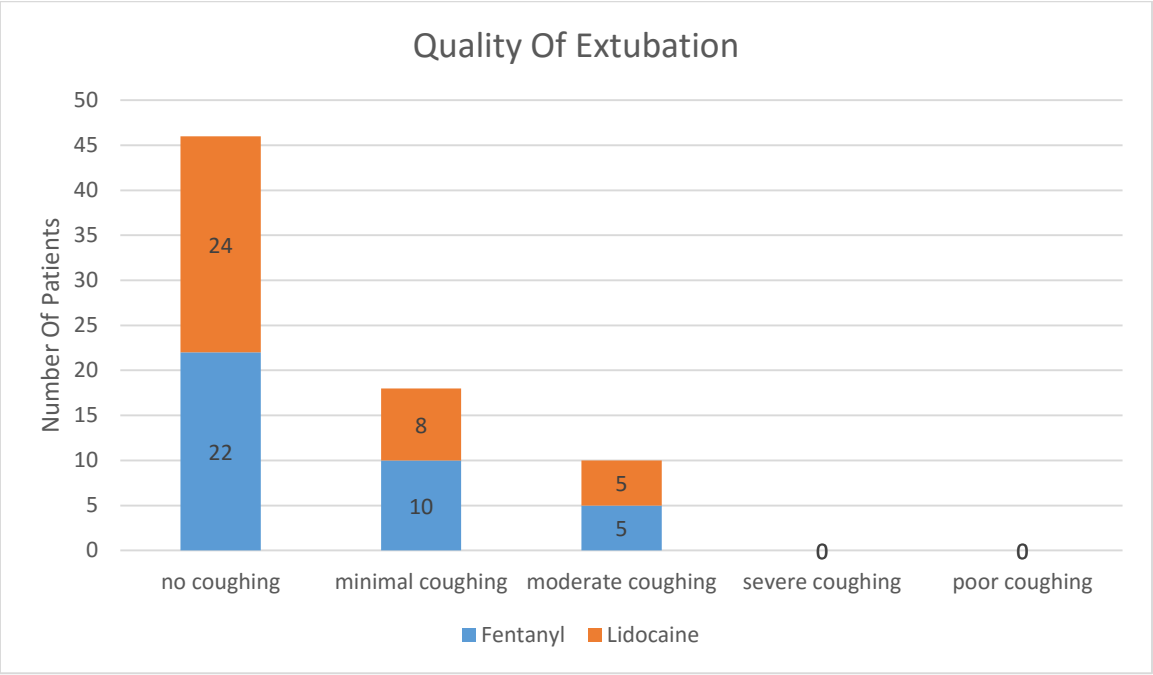



Figure 2: Grading of coughing during extubation between lidocaine and fentanyl groups patients who underwent ENT surgeries in Yekatit 12 Hospital Medical College, January 01 to March 30, 2018.

## 5.2 Discussion

Extubation of the trachea should be devoid of significant changes in hemodynamic parameters and adverse events, such as coughing, breathe holding, or laryngospasm. The receptors, particularly in the larynx, trachea and bronchi, are stimulated by mechanical and chemical factors during extubation as in laryngoscopy and intubation, which produces cardiovascular and respiratory reflex responses. During laryngoscopy, intubation, and extubation, the plasma concentrations of noradrenaline and adrenaline causing tachycardia and hypertension which may result in complications such as cardiac failure, pulmonary edema, and cerebrovascular hemorrhage (3).

Fentanyl acts at opioid receptors and predominantly acts on μ receptors. It decreases sympathetic tone and increases parasympathetic tone. Low doses of fentanyl were employed because a large dose can lead to muscular rigidity, bradycardia, nausea and vomiting postoperative respiratory depression(4).

Lidocaine attenuates the hemodynamic response to tracheal extubation by its direct myocardial depressant effect, central stimulant effect, and peripheral vasodilatory effect and it also suppresses the cough reflex, an effect on synaptic transmission. So we had considered lidocaine in our study(5).

Our study demonstrate there was statistically significant difference in mean HR 1 min after extubation with p value of 0.024. There was also a statistically significant difference 1 min after extubation ($p < 0.0001$). There was statistically significant difference in mean PR and MAP at 5 and 10 min after extubation ($p < 0.05$).

A randomized control study in India shows similar finding to our study observed that heart rate was significantly lower in fentanyl group compared with the control group ($p<0.0001$) (22). The likely explanation for the similarity may be the dose of fentanyl and time of administration of the study drugs were the same.

In line with our result Gurulingappa et al. compared Between IV Bolus Fentanyl and Lidocaine efficacy on hemodynamic stability and revealed that HR was significantly greater in lignocaine group than in fentanyl group ($p<0.05$). BP was also statistically significant in lignocaine group than in fentanyl group ($p<0.05$) in patients scheduled for elective surgical procedures (4). Another study conducted by Kumar et al. shows comparable result to our finding. This study compared fentanyl and fentanyl plus lidocaine on attenuation of hemodynamic stress response to laryngoscopy in controlled hypertensive patients posted for laparoscopic cholecystectomy. The mean heart rate 1 min after intubation with mean ± SD is 78.26 ± 8.92 and 72.16 ± 8.94 in fentanyl group and fentanyl with lidocaine group respectively with p value of 0.80 (11).

A randomized control trial conducted by Savitha et al observed thatcompared 0.5mg/kg of IV lignocaine with 1mg/kg of IV lignocaine for attenuation of hemodynamics response to extubation. Mean arterial pressures attenuation with lignocaine 1mg/kg found to be superior when compared to saline group ($P<0.001$). There was no significant difference in heart rate attenuation between patients who received 0.5mg/kg and 1 mg/kg lidocaine at 1min with p value of 0.101 (5). The difference to our study may be due to study participants were all elective surgeries under GA, which includes patients scheduled for General Surgery, Orthopedic, Gynecological, Plastic and Neurosurgical procedures, therefore, there is no manipulation of the airway by the surgeon.

In our study there was no statistically significant difference between two groups with decreasing the incidence of coughing in the Periextubation period with a p value of 0.857.

Indian study shows a comparable result to our finding. Ten minutes prior to extubation, patients were infused with 0.9% normal Saline, Fentanyl 1μg /kg and Dexmedetomidine 1μg /kg over 10 minutes period. The extubation quality in Fentanyl group had statistically significant lower scores compared to saline group ($p<0.001$) which shows better quality of extubation (22).

Khezri et al. shows 1.5 mg/kg intravenous lidocaine effects on bucking, cough, and emergence time at the end of anesthesia. Mild cough following extubation was observed in 4(3.3%) patients of groups IV lidocaine group. No case with moderate or severe cough was detected. There was no significant difference in incidence of cough during the thirty minutes after extubation between two groups (P=0.97). When we compared this result to our finding the proportion of coughing was lower (24). This may be due to study participants were elective minor orthopedic surgery, lower abdominal surgery or gynecological surgery but in our study there was a shared airway between the anesthetist and the surgeon in the perioperative period which makes the airway more irritant.

# 6. STRENGTH AND LIMITATION

## 6.1 Limitation of the Study

Lack of similar literatures in similar area.

Difficult to get enough similar studies

Most studies we used for comparison were randomized control trial.

## 6.2 Strength of the Study

Study participants were homogenous between lidocaine and fentanyl groups.

We had got the required sample size during the study period.

# 7. CONCLUSION AND RECOMMENDATION

## 7.1 Conclusion

The findings of our study demonstrate that fentanyl l μg/kg IV administered 10 min before the end of operation was effective in attenuating hemodynamic response to tracheal extubation when compared to lidocaine 1.5 mg/kg IV in patients underwent ENT surgeries.

## 7.2 Recommendation

We recommend that fentanyl administered 10 minutes before the end of operation for ENT surgeries is effective in attenuating hemodynamic response to extubation.
We also recommend additional randomized controlled study.

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# Annex I. Consent form

Addis Ababa University College of health Sciences, School of graduate studies, Department of anesthesia. Questionnaire prepared to compare the effectiveness of fentanyl and lidocaine on attenuation of hemodynamic response to extubation.

This questionnaire is to be used as a guide to collect information for the data collectors.

Hello! My name is ----------I am one of the members of the research team. The purpose of this questionnaire is to gather information on controlling hemodynamic response to extubation. I have identified you as a study participant hoping that you would be willing to help me by providing with some information. I have some questions which I would like to fill from your chart and postoperative data monitoring screen if you are willing. All information on your chart and data monitoring screen provide will be kept confidential. I will not include such as your name or exact address. Only honest data would contribute to improvement of health planning. Your role in the success of the research is important and I appreciate your contribution to the research. The researcher explained the aim of the study and to decide any time if I do not want to participate. So I assure that my interest to participate in this study is truly from my knowledge.

Are you voluntary to participate in the study?

A. Yes ☐

B. B. No ☐

If Respondents are voluntary to participate, the data collection will be started. For any question or concerns you can contact the principal investigator using the following address.

Phone number: 0966261787

Gmail: ephfen2007@gmail.com

Thank you!

**ሰላም ክቡራትና ክቡራን**

ስሜ _____ እባላለሁ።

እኔ በአዲስ አበባ ዩኒቨርሲቲ በአንስቴሽያ ት/ት ሳይንስ የማስትሬት ድግሪ ተማሪ የመመረቅያ ፅሁፉን ቀዶ ህክምናዉ ካለቀ በኋላ በጉሮሮ ዉስጥ የገባዉ ቱቦ በሚወጣበት ወቅት የሚከሰቱ ችግሮችን ለመቅረፍ ለህሙማን በሚሰጥ መድሐኒት ዙርያ በሚቀርብ ጥናት ተሳታፊ ነኝ። ከዚሁ ጥናት የሚገኘዉ መረጃ የጤና ባለሙያዎች በጥሩ ሁኔታ በሽተኞችን እንዲረዱ ያግዛቸዋል።

ስለዚህ የእርስዎ በጥናት ዉስጥ መካትተ ለዚህ ጥናት መሳካት ከፍተኛ አስተዋጾ አለዉ።

ከእርስዎ የምናገኘዉ ማንኛዉም መረጃ ለምርምር አገልግሎት እንደሚዉል እየገለጽኩኝ በማንኛዉም ሁኔታ የእርስዎ የግል መረጃ ለሌላ አገልግሎት እንደማይዉል ለማሳሰብ እወዳለሁ።

ለመቀጠል ይፈልጋሉ?

አዎ…….

አልፈልግም……..

(ስለ ዕርዳታዎ በቅድሚያ ላቅ ያለ ምስጋና አቀርባለሁ።)

**የአጥኝዉ ስምና አድራሻ**

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ኢሜይል፡ **ephfen2007@gmail.com**

አመሰግናለሁ!

Medical Registration No……

## Annex II. Questionnaires

### I. Demographic data

| Serial no. | Question | Response | Code |
|---|---|---|---|
| 101 | Age(yrs.) | | |
| 102 | Sex(M/F) | A. Male<br>B. Female | |
| 103 | ASA(I/II) | A. ASA I<br>B. ASA II | |
| 104 | BMI(kg/cm$^2$) | ------- | |

### II. Data during preoperative period

| Serial no. | Question | Response | Code | |
|---|---|---|---|---|
| 201 | Is there any coexisting medical disease | 1. YES 2. NO | | If no skip to No. 203 |
| 202 | If yes, specify the disease | | | |
| 203 | Diagnosis | | | |
| 204 | Planned surgical procedure | | | |
| 205 | Type of drug used before induction | A. Paracitamol<br>B. Diclofenac<br>C. Tramadol<br>D. Dexamethasone<br>Other, specify | | |

### III. Data during in the intraoperative period

| Serial no. | Question | Response | Code | |
|---|---|---|---|---|
| 301 | Induction agent type and dose | Thiopental ----------mg<br>Propofol ----------mg<br>Diazepam ----------mg<br>Suxamethonium----------mg<br>Vecuronium ----------mg<br>Pancuronium----------mg<br>Halothane----------<br>MAC | | |
| 302 | Number of attempts to intubate | | | |
| 303 | Internal diameter of the ETT(mm) | | | |
| 304 | Maintenance of Anesthesia | Halothane<br>Isoflurane<br>Pancuronium---------mg<br>Suxamethonium-----mg<br>Vecuronium---------mg | | |
| 305 | Additional Intraoperative analgesia given | 1. YES 2. NO | | If no skip to No. 307 |
| 306 | If YES specify type and dose | _____,_____mg | | |
| 307 | Type and doses of drug used before extubation | A. Lidocaine----mg<br>B. Fentanyl-----mg | | |
| 308 | Experience of anesthetist(yrs.) | | | |
| 309 | Experience of surgeon | A. R3<br>B. R4<br>C. Senior | | |
| 310 | Estimated intraoperative blood loss(ml) | | | |

| | | | | |
|---|---|---|---|---|
| 311 | Amount of fluid used in the intraoperative period(ml) | | | |
| 312 | Duration of surgery(min) | | | |
| 313 | Duration of anesthesia(min) | | | |
| | | | | |

## IV. Hemodynamic parameters

| Serial no. | V/S | Before anesthesia | Before study drug administration(10min before end of operation) | After the study drug administration(5 min before end of operation) | 1 min after extubation | 5min after extubation | 10 min after extubation | 15 min after extubation |
|---|---|---|---|---|---|---|---|---|
| 401 | HR | | | | | | | |
| 402 | SBP | | | | | | | |
| 403 | DBP | | | | | | | |
| 404 | MAP | | | | | | | |
| 405 | SPO2 | | | | | | | |

## V. Extubation quality

| Serial no. | Question | Response | Code |
|---|---|---|---|
| 501 | Number of coughing | | |
| 502 | Any complication after extubation | A. Desaturation<br>B. Breath holding<br>C. Laryngospasm<br>D. Specify, if others | |

# Annex III. Declaration

I, the undersigned, declare that this thesis is my original work in partial fulfillment of the requirements for the degree of MSc in Advanced Clinical Anesthesia. I understand that plagiarism will not be tolerated and all directly quoted material has been appropriately referenced.

Name: _____

Signature: _____

Submission to MSc Tutor, Dept. of Anesthesia, Addis Ababa University.

Date of Submission: _____

This thesis work has been submitted for examination with my/our approval as Advisors and Tutors on the MSc in Advanced Clinical Anesthesia course

Name Signature

1. _____ _____

2. _____ _____

3._____ _____