

COMPARISON OF THE EFFECT OF TWO DIFFERENT DOSES OF PROPOFOL IN ATTENUATION OF HEMODYNAMIC AND COUGH RESPONSE TO TRACHEAL EXTUBATION AMONG ADULT ELECTIVE SURGICAL PATIENTS AT JIMMA MEDICAL CENTER, ETHIOPIA 2022



INVESTIGATOR: FIKIRTE MAMO (BSC)

A THESIS REPORT TO BE SUBMITTED TO JIMMA UNIVERSITY
INSTITUTE OF HEALTH FACULTY OF MEDICAL SCIENCE
DEPARTMENT OF ANESTHESIA IN PARTIAL FULFILMENT FOR THE
REQUIREMENT OF MASTERS DEGREE IN ANESTHESIA

Tittle of the research	Comparison effect of two different doses of propofol on attenuation of hemodynamic and cough response to tracheal extubation among adult elective surgical patients at Jimma medical center, Ethiopia
Name of the investigator	Fikirte Mamo (Anesthesia MSc student)
Name of advisors	<ol style="list-style-type: none">1. Mr Bayisa Bereka (BSc, MSc, Assistant professor of PCHN),2. Mr Abebe Dukessa (BSc, MSc) ,3. Mr Melka Biratu (BSc, MSc)
Date	December 2022, Jimma Ethiopia

ABSTRACT

Background: Tracheal extubation is the purposeful removal of the endotracheal tube from the trachea. The act of extubation itself is physiologically stressful and is often accompanied by significant hemodynamic changes and respiratory tract complications. Extubation induced hemodynamic and cough response gives less attention by anesthesia professionals and the practice of using appropriate dose of propofol for attenuation of hemodynamic response during extubation lacks uniformity among anesthesia professionals.

Objective: The objective of the study was to compare the effect of two different doses of propofol on attenuation of hemodynamic and cough response during extubation among adult elective surgical patients from August 2022 to December 2022 at Jimma medical center.

Methods : A comparative cross sectional study were conducted on 102 adult elective surgical patients ages between 18 and 65 who required orotracheal intubation and randomly allocated to control group (n=34), propofol 0.5mg/kg (n=34) and propofol 1mg/kg (n=34). Hemodynamic parameters like heart rate, systolic blood pressure and mean arterial blood pressure were recorded just before residual effects of muscle relaxants were reversed as a baseline value and 1st, 3rd, 5th and 10 minute after extubation. Cough response following extubation was graded as (grade 0, 1, 2 and 3). The hemodynamic parameters were analyzed using one way ANOVA, Post hock –Tukey test, Student unpaired t-test and chi square test and p- value < 0.05 were considered statistically significant.

Result: The socio-demographic and clinical characteristics of the respondents were not statistically significant. There were a significant difference between control and propofol groups but there were no statistical significant difference between the two doses; both are effective on attenuation of hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) at 1st, 3rd, 5th and 10 minutes and cough response after extubation.

Conclusion: There were no significant difference between the two doses. Both intravenous propofol 0.5mg/kg and 1mg/kg when given prior to extubation were effective on attenuation of hemodynamic parameters and cough response following extubation. Anesthetists might consider low dose propofol 0.5mg/kg for attenuation of hemodynamic and cough response to endotracheal extubation. **Key words:** Propofol doses , attenuation effect, and cough response.

Contents	Pages
ABSTRACT.....	ii
LISTS OF ABBREVIATIONS.....	iv
LISTS OF TABLES.....	v
ACKNOWLEDGMENT.....	vi
CHAPTER ONE: INTRODUCTION.....	7
1.1 BACKGROUND.....	7
1.2 STATEMENT OF PROBLEM.....	7
1.3 SIGNIFICANCE OF THE STUDY.....	12
CHAPTER TWO: LITERATURE REVIEW.....	13
2.1 Propofol for attenuation of hemodynamic response during extubation.....	13
CHAPTER THREE: OBJECTIVES.....	16
3.1 General Objective.....	16
3.2 Specific Objective.....	16
CHAPTER FOUR: METHODS.....	17
4.1. Study area and period.....	17
4.2. Study design.....	17
4.3 Population.....	17
4.3.1 Source population.....	17
4.3.2 Study population.....	17
4.4 Sample size and sampling technique.....	18
4.4.1 Sample size.....	18
4.4.2 Sampling technique.....	19
4.5 Data collection technique and procedure.....	19
4.6 Eligibility Criteria.....	20
4.6.1 Inclusion criteria.....	20
4.6.2 Exclusion criteria.....	20
4.7 Study Variables.....	21
4.8 Operational definition.....	22
4.9 Data analysis method.....	24

4.10 Data quality assurance.....	25
4.11 Ethical Consideration	25
4.12 Dissemination plan.....	25
CHAPTER FIVE: RESULTS.....	26
5.1 Demographic status and clinical characteristics of the respondents among groups	26
5.2 Comparison of attenuation of hemodynamic response among groups	28
5.2.1 Comparison of heart rate among groups.....	28
5.2.2 Comparison of systolic blood pressure among groups.....	29
5.2.3 Comparison of diastolic blood pressure among groups.....	30
5.2.4 Comparison of mean arterial pressure among groups	31
5.2.4 Comparison of cough response during extubation among groups	31
CHAPTER SIX: DISCUSSION	34
CHAPTER SEVEN: CONCLUSSION AND RECOMENDATION.....	41
7.1 Conclusion.....	41
7.2 Recommendations	41
7.3 Limitation of the study	41
REFERENCES	41
Annex I: Consent form and questionnaire	44

LISTS OF ABBREVIATIONS

JUMC	-----	Jimma university medical center
ASA	-----	American Society of Anesthesiology
BMI	-----	Body Mass Index
BP	-----	Blood Pressure
ETTI	-----	Endotracheal Tube Intubation
GA	-----	General Anesthesia
HR	-----	Heart Rate
SBP	-----	Systolic blood pressure
DBP	-----	Diastolic blood pressure
MAP	-----	Mean arterial blood pressure
NIBP	-----	Noninvasive blood pressure
ENT	-----	Ear, nose, throat
IV	-----	Intravenous
Kg	-----	Kilo gram
Min	-----	Minute
MmHg	-----	Millimeter mercury
RCT	-----	Randomized Controlled Trial
PI	-----	principal investigator

LISTS OF TABLES

Table 1. Demographic status and clinical characteristics of patients who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Table 2. Comparison of mean heart rate among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Table 3. Comparison of mean systolic blood pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Figure 1. Comparison of mean diastolic blood pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Figure 2. Comparison of mean arterial blood pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Figure 3. Comparison of the occurrence and grade of cough during extubation among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

ACKNOWLEDGMENT

First, I would like to thank Jimma university institute of health faculty of medical science department of anesthesia for providing me the chance to prepare this research thesis. Secondly my appreciation goes to my advisors Mr Abebe Dukessa, Mr Bayisa Bereka and Mr Melka Biratu for their constructive comments throughout this thesis work.

Also I would like to thank study participants and data collectors.

CHAPTER ONE: INTRODUCTION

1.1 BACKGROUND

Tracheal extubation is the discontinuation of an artificial airway when the indications for its placement like airway obstruction, protection of airway, suctioning, ventilatory failure and hypoxemia no longer exist (Bindu *et al.*, 2013). Tracheal extubation is a critical step during emergence from general anesthesia. It is not simply a reversal of the process of intubation because conditions are often less favorable than at the start of anesthesia (Mitchell *et al.*, 2012).

The act of extubation itself is physiologically stressful and is often accompanied by significant hemodynamic changes and respiratory tract complications (Wong, Weber and Abramowicz, 2021). For a smooth extubation, there should be no straining, movement, coughing, breath holding or laryngospasm (Fuhrman *et al.*, 1992). Extubation at light levels of anesthesia or sedation can stimulate reflex responses via tracheal and laryngeal irritation (Bindu *et al.*, 2013). There is an increase in the concentrations of noradrenaline and adrenaline in the plasma due to the stimulations which affect various cardiovascular and airway responses (Nigussie *et al.*, 2021).

Tracheal extubation as well as intubation often provokes cardiovascular changes with marked increases in heart rate and arterial blood pressure. These hemodynamic changes during extubation are probably of little consequence in healthy individuals, but may be more severe and more dangerous in hypertensive patients (Fujii *et al.*, 1999). During extubation, massive catecholamine release secondary to suctioning and stimulation leads to an increase in blood pressure, heart rate, intraocular pressure, and intracranial pressure (Nigussie *et al.*, 2021).

Extubation irritates airways, causing cough or strain, both of which are known to increase blood pressure and heart rate. Coughing on emergence from general anesthesia is virtually ubiquitous, particularly when an endotracheal tube is used (Nishina *et al.*, 1995; Jung, Park and Kim, 2014).

Although coughing is a protective reflex, it can be particularly troublesome in the setting of ophthalmologic, neurologic, oropharyngeal, and neck surgery (Cooper and Khan, 2012).

1.2 STATEMENT OF PROBLEM

Tracheal intubation receives much attention and tracheal extubation has received relatively little emphasis. The scope and significance of problems occurring after tracheal extubation are real (Nagrале, Indurkar and Pardhi, 2016). In the context of extubation, adverse events can be sorted into three major categories: respiratory, traumatic, and hemodynamic. Many of these adverse events can result in the depletion of oxygen stores at extubation, resulting in postoperative hypoxia. In severe cases, hypoxia can lead to hypoxic brain injury, cardiovascular injury, and possibly death (Wong, Weber and Abramowicz, 2021). During tracheal extubation, stimulation which affects hemodynamic changes is multifactorial; e.g., pain of the wound, emergence from anesthesia, or tracheal irritation (Nishina *et al.*, 1995).

Emergence from anesthesia and extubation can provoke a stressful response, resulting in tachycardia and hypertension (Fuhrman *et al.*, 1992). Even though the elevation in blood pressure and heart rate due to extubation are brief, they may have detrimental effects in high risk patients (Nagrале, Indurkar and Pardhi, 2016). This response may lead to increased morbidity and life threatening complications in patients with intracranial and cardiovascular problems (Bostan and Eroglu, 2012).

Laryngeal, tracheal and bronchial receptors are stimulated by mechanical and chemical irritants during laryngoscopy, intubation and extubation. The reflex increase in sympatho-adrenergic activity caused by these manipulations leads to an increase in catecholamine release, arterial blood pressure and heart rate. Tracheal extubation is a stressful phenomenon, which can release these chemical substances (Bostan and Eroglu, 2012; Salim *et al.*, 2019).

Extubation irritates airways, causing cough or strain, both of which are known to increase blood pressure and heart rate (Nishina *et al.*, 1995). Many investigators have documented that tracheal extubation causes modest (10%-30%) and transient increases in blood pressure and heart rate, lasting 5-15 minutes. Coriat *et al* demonstrated that patients with coronary artery disease experience significant decreases in ejection fractions (from $55\% \pm 7\%$) to ($45\% \pm 7\%$) after extubation (Miller, Harkin and Bailey, 1995).

Many strategies have been advocated to minimize these hemodynamic adverse responses such as; block of superior laryngeal nerve, fentanyl, morphine, lignocaine, β -blockers, calcium

channel blockers, hydralazine, and low dose propofol. But they all have limitations and side effects. None of these control methods is perfect: anesthesia may be prolonged, the treatment may be ineffective, respiration may be depressed (Fuhrman *et al.*, 1992; Bindu *et al.*, 2013; Nagrale, Indurkar and Pardhi, 2016).

Respiratory complications may be frequent during and after tracheal extubation (Asai, Koga and Vaughan, 1998). In the clinical practice respiratory complications after tracheal extubation are three times more common than during tracheal intubation and induction of anesthesia (12.6% vs 4.6%) (k.S savitha, D'souza Joylin Stephany, 2014). The incidence of complications immediately after tracheal extubation was significantly higher than that during induction of anesthesia and the most common was coughing (6.6%) (Asai, Koga and Vaughan, 1998).

The incidence of post- extubation coughing reported in different studies was between 76% and 96%. Extubation can stimulate unwanted airway responses due to laryngeal and tracheal irritation leading to cough, laryngospasm, and bronchospasm. These airway and circulatory responses on extubation can lead to surgical bleeding, cardiovascular instability, and respiratory compromise (Salim *et al.*, 2019).

Coughing during emergence of general anesthesia is a physiologic response to tracheal extubation which can result in potentially dangerous patient movements, hypertension, tachycardia or other arrhythmias, myocardial ischemia, bleeding from surgical site , disruption of surgical wounds from excessive movement ,bronchospasm, and an increase in intracranial and intraocular pressures (Khezri, Asefzadeh and Kayalha, 2011; Jung, Park and Kim, 2014).

During awakening from endotracheal anesthesia, the trachea may be stimulated by the endotracheal tube, by noxious effects of the anesthetic gas itself, or by un cleared secretions (Kim and Bishop, 1998). It is widely believed that approximately 82.5% of patients experience a cough upon emergence from general anesthesia with causes possibly including the presence of an endo- tracheal tube, un cleared secretions and anesthetic gas (Hu *et al.*, 2019) .

Techniques that have been used to help diminish coughing during emergence include "deep" extubation (removal of the endotracheal tube while the patient is still in a deep plane of general anesthesia), administration of intravenous narcotics, or administration of intravenous lidocaine prior to emergence (Gonzalez *et al.*, 1994).

Current strategies include extubation on low-dose propofol or remifentanyl and intracuff or intravenous lidocaine, which may reduce coughing and straining on extubation (Cooper and Khan, 2012). Propofol is a potent intravenous hypnotic agent with antioxidant anti-inflammatory and bronchodilating properties (Marik, 2005). Propofol is used widely in clinical anesthesia and it is known to be an inhibitor of airway reflexes (Jung, Park and Kim, 2014). Propofol can decrease systemic vascular resistance and cardiac contractility which leads to a decrease in heart rate and blood pressure (Nigussie *et al.*, 2021).

Propofol has a rapid onset of action with a dose-related hypnotic effect. Propofol is rapidly redistributed and eliminated following a single bolus injection. Its elimination half-life is 4-23 hrs. However, its duration of clinical effect is much shorter, because propofol is rapidly distributed into peripheral tissues (Marik, 2005).

When used for intravenous sedation, a single dose of propofol typically wears off within minutes (Marik, 2005; Cheng *et al.*, 2011). Propofol has been reported to have many pharmacological effects: it reduces cerebral blood flow, cerebral metabolic rate, and intracranial pressure (Kotani *et al.*, 2008). The ability of propofol to reduce blood pressure is associated with a decrease in systemic vascular resistance (15%-20%) and stroke volume index ($\pm 20\%$) (Moein Vaziri *et al.*, 2013). The reported adverse effects of propofol are: pain on injection, bradycardia, arterial hypotension, blood- stream infection, airway obstruction, changes in serum lipids, and excitation of the central nervous system (Kotani *et al.*, 2008).

Different studies which is done with different dose of propofol shows that there is a controversies regarding the effects of propofol on the attenuation of hemodynamic response during extubation and using small dose of propofol for example propofol dose 0.3mg/kg may not result to have an intended effect on prevention of extubation induced hemodynamic and cough response in which the patient may not be benefited and increments of those events during extubation will result in morbidity and mortality to the patient.

In contrast ideally using of higher dose of propofol during extubation to prevent those events is associated with increased postoperative side effects like hypotension, respiratory depression and postoperative sedation which will increases postoperative recovery time, hospital stay and increased cost of the patient and hospitals.

A previous study which is conducted in our country, Asella teaching and referral hospital on attenuation of hemodynamic response to tracheal extubation with propofol dose 0.5mg/kg shows that it decreases hemodynamic response to tracheal extubation but there is a paucity of information about the effects of propofol on attenuation of extubation induced cough in which this study will fill this gap.

Even though extubation induced hemodynamic changes are preventable, if left untreated it will result in untoward physiologic side effects to the patient which may result in morbidity and mortality.

Some of the problems against the act of attenuating hemodynamic and cough reflex during extubation are; lack of drugs at every setup, lack of attention towards the importance of hemodynamic stabilization, side effects of drug, inadequate literatures on hemodynamics and cough reflex secondary to orotracheal suctioning and extubation.

In foreign country few studies showed the effect of propofol on attenuation of extubation induced hemodynamic changes with different success rate and in sub- saran country literatures shows that there is a limited even a paucity of information about the effects of proppofol on attenuation of hemodynamic response following extubation.

Even though extubation induced hemodynamic and cough response complications unless prevented with pharmacologic strategies or deeper extubation techniques, the patient may end up with poor outcome of surgery, which may not be detected immediately but causes long lasting problems to the patients. Propofol is widely available drug in our country many hospital setup even in a resource limited setup but there is a limited information about its effect on attenuation of hemodynamic changes during extubation and from my routine clinical practice observation because there is no standardize dose of propofol, for attenuation of hemodynamic response during extubation most of the anesthesia professionals uses different doses of propofol for attenuation of hemodynamic and cough response during extubation. Therefore the aim of this study is to compare the effects of two different doses of propofol on attenuation of hemodynamic and cough response during extubation so that in order to get effective clinical dose of propofol that prevent problems associated with hypertension, tachycardia and coughing during extubation especially in hospitals where newly introduced drugs such as fentanyl, esmolol, magnesium sulphate are not easily accessible.

1.3 SIGNIFICANCE OF THE STUDY

Studying the effect of propofol on hemodynamics and cough response as well as comparing the two doses and specifying it is expected to contribute on techniques and methods used to avoid problems associated with emergence and extubation, especially patients with neurological surgery, coronary artery disease, hypertensive patients and all surgical patients in whom tachycardia, hypertension, coughing, bucking or straining during emergence are not desirable are beneficiary from this study.

Extubation induced hemodynamic and cough response gives less attention by anesthesia professionals and from the routine clinical practice observation the practice of using appropriate dose of propofol for attenuation of hemodynamic and cough response during extubation lacks uniformity among anesthesia professionals.

Since the main objective of this study is to compare the effects of two different doses of propofol on attenuation of hemodynamic response during extubation the result will:

- ✓ Be used as a base line information and input for anesthesia clinical practice
- ✓ Motivate the anesthesia professionals to use propofol uniformly in their patient management protocols so as increase quality of care.
- ✓ Improves the outcomes of patients by reducing unavoidable extubation induced complications and
- ✓ Give supportive information for the scientific community.

As far as my knowledge there is no research conducted in my study area before so this study will be used as evidence for further research which will be conducted on the same topic as well as related topics.

The study also will help generate information that may help program planners to develop effective preventive strategies, to select the best alternative solutions and to evaluate effectiveness of implemented preventive interventions targeted to the problem.

CHAPTER TWO: LITERATURE REVIEW

2.1 Propofol for attenuation of hemodynamic response during extubation

A study conducted by Sarabjit Kaur in India in 2006 on 50 elective patients whose age was between 4 and 14 years to assess the role of propofol in prevention of extubation related complications in oral surgery with propofol dose 1mg/kg and control group. The result shows propofol 1mg/kg causes a fall in heart rate and systolic blood pressure which was statistically significant ($P < 0.05$) but a significant reduction in diastolic blood pressure wasn't observed and bucking on extubation were observed in 3 patients (12%) which was statistically significant (Kaur *et al.*, 2006).

A study done in the Third Hospital of Chinese People's Liberation Army and Xijing Hospital of Fourth Military Medical University on the effects of propofol (1.5mg/kg) versus urapidil (2.5mg/kg) on perioperative hemodynamics and intraocular pressure during anesthesia and extubation in ophthalmic patients on total of 82 surgical patients aged between 24 and 65. The result shows; In propofol group, the blood pressure and heart rate between extubation and thereafter, no significant difference were found compared with those before induction, while there were significantly lower than those before giving propofol (< 0.05). The incidence of cough were less in propofol group (Cheng *et al.*, 2011).

Another a randomized control trial (RCT) study done in Iran on 2013 among 80 patients with ASA physical status I, undergoing an elective surgery with propofol does 0.5mg/kg and control group 2min before extubation. The result shows there were no any significant changes seen in cough production between the two groups and propofol can reduce systolic blood pressure, diastolic blood presurre, mean arterial pressure and heart rate and cough production at the time of injection but there were no significant changes in these parameters after extubation (Moein Vaziri *et al.*, 2013).

A randomized control trial (RCT) study done in Busan, Korea (2014) on the effect of a sub hypnotic dose of propofol for the prevention of coughing in adults during emergence from anesthesia on 60 patients aged b/n 18-65 years, undergoing elective nasal surgery under general anesthesia with propofol dose 0.3mg/kg and control group the result shows the incidence and grade of coughing during emergence was significantly lowered in the propofol group compared to their control group. There were no significant changes seen in heart rate and mean arterial pressure. The results were considered to be because only a small dose of propofol was used in the study (Jung, Park and Kim, 2014).

A randomized control trial (RCT) study done in Egypt on 2015 on comparison of small dose of Propofol (0.8mg/kg) and Midazolam (0.05mg/kg) in preventing of laryngospasm and coughing following extubation during oropharngal surgery among adult patients, the result shows after tracheal suction and up to first 5 minute after extubation propofol significantly decreases blood pressure and increase pulse rate in comparison with the base line value and the incidence and grade of coughing during emergence was significantly lowered by propofol (Shaban, 2015).

In Telangana, India in 2016, a prospective randomized study was done on 90 patients age between 20 and 50 years to evaluate hemodynamic effects of intravenous propofol dose 0.5mg/kg, intravenous lignocaine and intravenous esmolol given two minutes prior to extubation and the result shows heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure significantly decreased in propofol and Esmolol group up to 10min after the study drug were given. The study concluded that propofol 0.5 mg/kg when given 2 minutes prior to extubation attenuates hemodynamic response to extubation immediately and satisfactorily and remained effective till 10 minutes post extubation, but causes sedation in postoperative period (Nagrle, Indurkar and Pardhi, 2016).

A study conducted by Konda Sunil in Telangana state India in 2018 on 60 adult elective surgical patients to evaluate the effects of intravenous propofol dose 0.5mg/kg and intravenous esmolol on attenuation of cardiovascular responses to tracheal extubation and the result shows; The decrease in mean heart rate, mean systolic blood pressure, mean diastolic blood pressure and mean arterial pressure were statistically significant in propofol group ($P < 0.05$) and propofol

0.5mg/kg were able to attenuate cough and strain of extubation in $\geq 95\%$ of patients (State, Author and State, 2018).

.In our country, Asella teaching and referral hospital a prospective cohort study conducted on comparison between intravenous lidocaine and propofol dose 0.5mg/kg administration on the attenuation of hemodynamic responses during extubation on 72 ASA I adult elective surgical patients. The result shows ; propofol 0.5mg/kg caused a reduction of heart rate at 1st, 3rd, 5th and 10 minutes, systolic blood pressure at 1st and 3rd minutes ,mean diastolic blood pressure at 1st, 3rd and 5th minutes and mean arterial pressure at 1st, 3rd and 5th minutes after extubation compared to lidocaine and their control group (Nigussie *et al.*, 2021).

CHAPTER THREE: OBJECTIVES

3.1 General Objective

To compare the effect of two different doses of propofol on attenuation of hemodynamic and cough response during extubation among adult elective surgical patients from August 2022 to December 2022 at Jimma medical center, Ethiopia

3.2 Specific Objective

- ✓ To compare the effect of two different doses of propofol on attenuation of hemodynamic response during extubation.
- ✓ To compare the effect of two different doses of propofol on attenuation of extubation induced cough response.

CHAPTER FOUR: METHODS

4.1. Study area and period

The study was conducted from July 2022 to November 2022 in Jimma medical center which is located in Jimma town, Oromiya regional state and is 350km south west of Addis Abeba. Currently it is the only teaching and referral hospital in the south western part of the country, providing services for approximately 16,000 inpatients, 220,000 outpatient attendants, 12,000 emergency cases and 4,500 deliveries in a year coming to the hospital from the catchment population of about 15 million peoples.

4.2. Study design

An institutional based prospective cohort study were conducted from August 2022 to December 2022. The comparison groups were group A control group (who did not received any medication), group B (who received propofol 0.5mg/kg) and group C (who received propofol 1mg/kg).

4.3 Population

4.3.1 Source population

All adult patients who were scheduled and underwent elective surgery under general anesthesia with endotracheal intubation at Jimma medical center during the study period.

4.3.2 Study population

All adult patients who were scheduled during study period for elective surgery under general anesthesia and fulfill inclusion criteria.

4.4 Sample size and sampling technique

4.4.1 Sample size

To determine sample size, the study used G* power version 3.1.9.2 software as a tool. As an input G* power requires selecting appropriate test family, type of statistical test with in test family, specifying α error probability, power (1- β error probability), and determining effect size. To calculate the effect size a simplified methodology by Thalheimer and cook was used, employing equation 1 and 2 (Kumar *et al.*, 2022).

$$d = \frac{M_1 - M_2}{SD_{pooled}} \quad \text{Eq. 1}$$

$$(1a) \quad S_{pooled} = \sqrt{\frac{(n_t - 1)s_t^2 + (n_c - 1)s_c^2}{n_t + n_c}} \quad \text{Eq. 2}$$

Where, d = Cohen's d effect size

M = mean score of groups (average of treatment or comparison conditions)

S = standard deviation

Subscripts; t refers to the treatment condition and c refers to the comparison condition (or control condition).

n = number of subjects

From previous study mean heart rate changes before and after extubation with propofol 0.5mg/kg and control group with mean and standard deviation (98.83 \pm 18.3, 94.8 \pm 13.98) and (95.6 \pm 15.15, 94.07 \pm 15.8) respectively were taken (Moein Vaziri *et al.*, 2013) and a calculated mean difference were 2.5, pooled standard deviation 4.8 and the effect size 0.52. A priori power analysis for one way ANOVA with three groups was conducted in G power considering alpha 5%, power 80% and allocation ratio 1 and the software found sample size 102. Adding 10% of

non-response rate a total of 102 patients were included in the study with 34 patients in each groups.

4.4.2 Sampling technique

Systematic random sampling technique were employed until to get the required sample size during the study period. The situational analysis was done at Jimma medical center by revising surgical and anesthetic records and shows that on average 3 adult elective surgical patients per day, 15 patients per week and 60 patients per month who full filled the inclusion criteria were operated on surgical log book.

According to this data there were 180 adult elective surgical patients on average 3months study periods from whom data were collected from only 102 patients. Therefore, $k = N/n = 180/102 \approx 2$ (skip interval) and the first study unit (random start) was selected using lottery method. Then, every two patients were included in this study from the daily operation schedule list.

4.5 Data collection technique and procedure

Mixed data collection method were employed including patient interview, document review, observation and measuring physiological response of hemodynamic parameters following extubation. Questionnaire was prepared in English and Affan oromo language which includes socio demographic characteristics of the patient, anesthesia and surgical characteristics of the patient, patient's hemodynamic parameters and patient's cough response following extubation.

The socio demographic, anesthesia and surgical characteristics of the patients were reviewed from patient's interview and patient's chart. The hemodynamic parameter were recorded before extubation , just before residual effects of muscle relaxants was reversed and prior to study drug administration as a base line value and 1, 3, 5 and 10 minutes after extubation from standard ASA monitors (pulseoximetry, electroencephalography and noninvasive blood pressure) and extubation induced cough response was graded as (grade 0,1,2 and 3).

After giving training data were collected by two BSC anesthetist under the supervision of 1 MSc anesthetist using a pretested check list. The principal investigator was supervised the completeness of the data daily. The data collector were record what anesthesia professional in charge administered propofol dose prior to extubation using prepared data collection tool.

The drug dose administered to the patient were recorded by observation, asking the anesthetist in charge and later checked from the anesthesia record sheet and anesthesia machine. The data were collected until the required number were reached.

4.6 Eligibility Criteria

4.6.1 Inclusion criteria

- ✓ ASA physical status I and II
- ✓ Airway assessment of mallampatti grade I & II
- ✓ Patient age between 18 and 65 years
- ✓ Patients BMI between 18.5 and 29.5
- ✓ Patients induced with ketamine and thiopentone
- ✓ Patients scheduled for elective surgeries under GA with ETT intubation; general surgery orthopedic surgery, and gynecological surgery

4.6.2 Exclusion criteria

- ✓ Patients who were allergic to the study drug
- ✓ Patients who have known history of difficult intubation
- ✓ Patients who were unwilling to participate in the study
- ✓ Patients on beta blockers
- ✓ Patients on Calcium channel blockers
- ✓ Patients those received propofol other than the intended time of the study
- ✓ Patients those received lidocaine before extubation
- ✓ Patients with coronary artery diseases
- ✓ Patients with history of active upper respiratory tract infections
- ✓ Patients with pulmonary diseases

4.7 Study Variables

Outcome variables

- ✓ Hemodynamic parameters and
- ✓ Cough response

Demographic and clinical characteristics related variables

- ✓ Age
- ✓ Gender
- ✓ BMI
- ✓ ASA physical status
- ✓ Mallampatti classification
- ✓ Duration of surgery
- ✓ Duration of anesthesia
- ✓ Procedure performed
- ✓ Induction agent used
- ✓ Intraoperative Opioid used
- ✓ Intubation trial

4.8 Operational definition

Endotracheal extubation: is removal of an endotracheal tube from the trachea which is performed in operating room.

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

ASA I: A normal healthy patients those have only surgical indication.

ASA II: Controlled medical conditions with mild systemic effect and no limitation of functional ability.

ASA III: A 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.

Attenuation of hemodynamic response : A reduction in hemodynamic responses (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure) which induced during endotracheal extubation.

Coughing: Is expelling air from the lungs with a sudden sharp sounds.

Attenuation of cough response: A reduction in cough response which induced during endotracheal extubation.

Grade of cough response during extubation;

Grade 0: No cough

Grade 1: Single cough with mild severity

Grade 2: Cough persistence less than 5 seconds with moderate severity

Grade 3: Severe, persistent cough more than 5 secondsThe scale was adopted from (Jung, Park and Kim, 2014)

Base line vital signs: Hemodynamics measured prior to the study drug administration and before extubation was defined as baseline value.

Hemodynamic parameters: Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure which were measured before study drug administration (base line) and 1 minute, 3 minute, 5 minute and 10 minute after extubation.

Elective surgery: is surgery done before on set (appearance) of any complication that might constitute urgent indication.

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 patient get response to verbal command.

Mallampatti is a technique used to predict ease of endotracheal intubation and classified as;

Mallampatti class I - when the soft palate, uvula and pillars are visible

Mallampatti class II – when the soft palate and the uvula are visible

Mallampatti class III - When only the soft palate and base of the uvula are visible

Mallampatti class IV - When only the hard palate is visible

4.9 Data analysis method

Once the data was collected and checked for completeness and consistency it was summarized and enter into Epidata computer program and coded for each category of variables then cleaned and analyzed with SPSS version 27 computer program. Hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial blood pressure prior to administration of the study drug and 1st, 3rd, 5th and 10 minutes after extubation and cough response following extubation were analyzed.

Analysis of one way ANOVA was used to find the significance of the study parameter between the three groups. Tukey post hock test was employed to make pairwise comparison between group means.

Results on continuous measurements were presented as mean \pm standard deviation. Significance was assessed at 5% level of significance. For analysis P-value < 0.05 was considered as statistically significant and P-value > 0.05 was considered as statistically not significant. Descriptive statistics, tables and figures were used to summarize the data.

4.10 Data quality assurance

To ensure the quality of data, training about the objectives and relevance of the study were given to data collectors and supervisors. During data collection follow up was done and cross check for completeness and consistency of data on daily basis. All materials used for data collection was arranged sequentially and data were stored in safe and secured place.

4.11 Ethical Consideration

Ethical clearance and approval were obtained from the ethical review committee of Jimma university institute of health science faculty of medical science. Permission to conduct the study were obtained from Jimma university medical center.

The purpose of the study was explained to patients under the study and written informed consent were obtained from each patients. The patients were informed that the care to be given wasn't compromised in any way and confidentiality was assured by avoiding identifiers and using codes to identify patients.

Name and other identifying information were not used in the study. Participant's 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 Jimma University, Jimma University Medical Center, and department of anesthesia. Possible efforts will be made to publish the results of the study to the international Journals.

CHAPTER FIVE: RESULTS

5.1 Demographic status and clinical characteristics of the respondents among groups

The demographic status like age, weight, height & BMI and the clinical characteristic's like duration of surgery and duration of anesthesia were comparable between the groups. There were no significant difference between the groups ($P>0.05$). (Table 1)

Table 1. Demographic status and clinical characteristics of patients who underwent elective surgery at Jimma medical center from August 2022 to December 2022

Variables		Group A (n =34)	Group B (n=34)	Group C (n=34)	P- value
Age (yr) (mean \pm SD)		49.09 \pm 5.10	46.47 \pm 7.2	47.59 \pm 7.17	0.28
Weight (kg) (mean \pm SD)		55.82 \pm 8.07	57.09 \pm 4.50	56.53 \pm 6.45	0.72
Height (meter) (mean \pm SD)		1.64 \pm .05	1.65 \pm .05	1.65 \pm .04	0.67
BMI (mean \pm SD)		20.70 \pm 3.43	20.80 \pm 1.43	20.77 \pm 2.44	0.98
Sex (n (%))	Male (n (%))	15 (44.1)	16 (47.1)	15(44.1)	0.96
	Female (n (%))	19 (55.9)	18 (52.9)	19 (55.9)	
Mallampatti classification (n (%))	Class I (n (%))	23 (67.6)	22 (64.7)	32 (94.1)	0.87
	Class II (n (%))	12 (35.3)	12 (35.3)	2 (5.9)	
ASA classification (n (%))	ASA I (n (%))	19 (55.9%)	21 (61.8)	28 (82.4)	0.75

	ASA II (n (%))	15 (44.1)	13 (38.2)	6 (17.6)	
Intubation trial (n (%))	First trial (n (%))	31 (91.2)	31 (91.2)	30 (88.2)	0.89
	Second trial (n (%))	3 (8.8)	3 (8.8)	4 (11.8)	
Types of surgery done (n (%))	General surgery (n (%))	27 (79.4)	25 (73.5)	29 (85.3)	0.51
	Orthopedic surgery (n (%))	3 (8.8)	5 (14.7)	3 (8.8)	
	Gynecology surgery (n (%))	4 (11.8)	4 (11.8)	2 (5.9)	
Induction agent used (n (%))	Ketamine	21 (36.2)	17 (50.0)	20 (58.8)	0.60
	Thiopentone	14 (41.2)	17 (50.0)	14 (41.2)	0.70
Duration of surgery (hr) (mean ± SD)		1.50±0.62	1.64±0.63	1.80±0.58	0.14
Duration of anesthesia(hr) (mean ± SD)		1.84±0.64	1.97±0.63	2.12±0.55	0.15
Intraoperative opioid used (n (%))		19 (55.9)	17 (50.0)	19 (55.9)	0.85

N.B: Group A= Control, Group B= Propofol 0.5mg/kg, Group C= Propofol 1mg/kg, SD= standard deviation, yr = year, hr = hour, kg =kilogram, BMI= body mass index, ASA= American society of anesthesiologist, n = number of patients, %= percent, P-value > 0.05 no significant difference

5.2 Comparison of attenuation of hemodynamic response among groups

5.2.1 Comparison of heart rate among groups

There were no significant difference among the groups in mean baseline heart rate ($P = 0.30$). There were a significant difference of heart rate between control (group A) and propofol groups (group B, and C) at 1st, 3rd, 5th and 10 minutes after extubation, however there was no significant difference of heart rate between propofol 0.5mg/kg (group B) and 1mg/kg (group C) at 1st, 3rd, 5th and 10 minutes after extubation. (Table 2)

Table 2. Comparison of mean heart rates among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

HR (beat per minute)	Group A (n= 34) Mean ± SD	Group B (n=34) Mean ± SD	Group C (n= 34) Mean± SD	P- value	Pairwise Significance		
					Group A vs Group B	Group A vs Group C	Group B vs Group C
Base line	93.71±5.40	92.41 ± 5.94	94.62±6.34	0.30	0.64	0.80	0.27
1 st minute after extubation	95.26±5.27	91.76 ±5.57	91.88±5.97	0.01	0.03	0.04	0.99
3 rd minute after extubation	96.29±6.38	88.29 ± 5.48	88.15±5.45	0.01	0.01	0.01	0.99
5 th minute after extubation	97.76±5.45	82.41±5.69	81.50±5.35	0.01	0.01	0.01	0.77
10 th minute after extubation	98.76±5.26	80.71± 5.26	79.74±3.27	0.01	0.01	0.01	0.67

N.B: HR= Heart rate, Group A= Control , Group B= Propofol 0.5mg/kg , Group C= Propofol 1mg/kg , SD= Standard deviation, n= number of patients, Vs= versus, P-value < 0.05 is statistically significant.

5.2.2 Comparison of systolic blood pressure among groups

There were no significant difference among the groups in base line mean systolic blood pressure (P =0.21). There were a significant difference of systolic blood pressure between control (group A) and propofol groups (group B, and C) at 1st, 3rd, 5th and 10 minutes after extubation, however there was no significant difference of systolic blood pressure between propofol 0.5mg/kg (group B) and 1mg/kg (group C) at 1st, 3rd, 5th and 10 minutes after extubation. (Table 3.)

Table 3. Comparisons of mean systolic blood pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

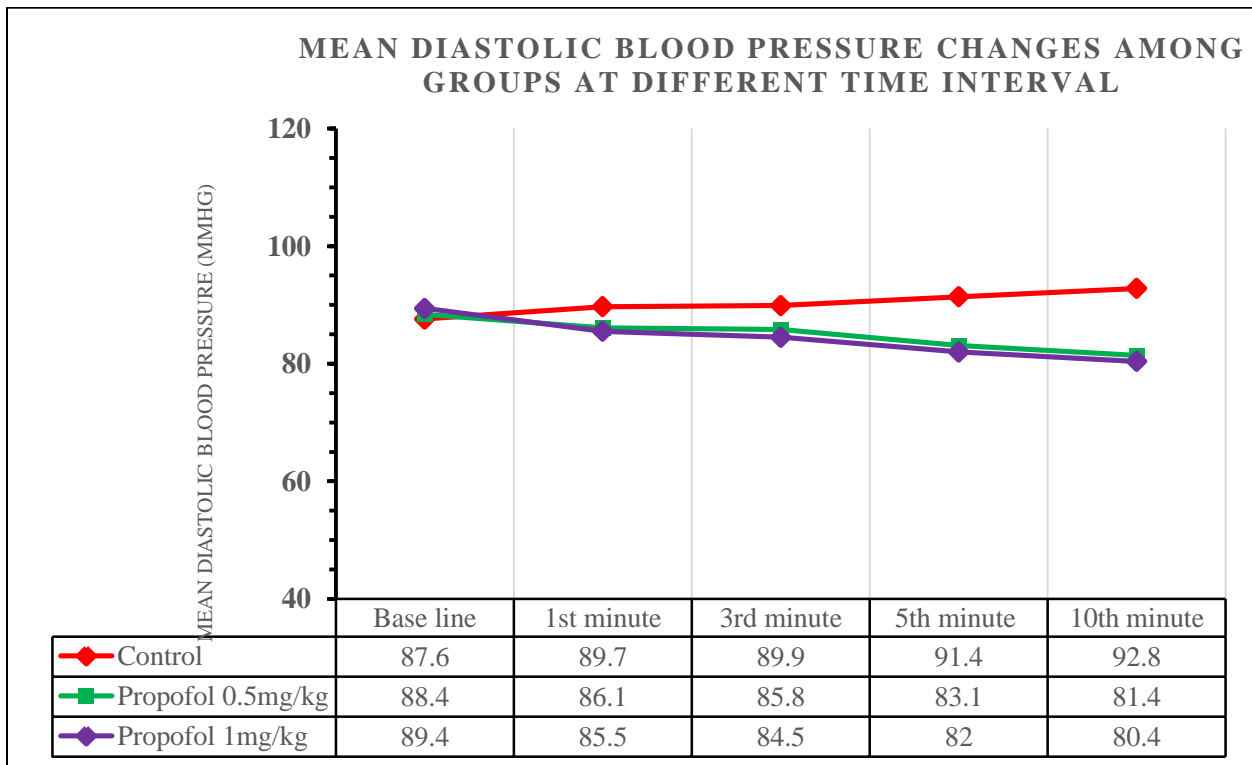
SBP (mmHg)	Group A (n= 34) Mean± SD	Group B (n=34) Mean ± SD	Group C (n= 34) Mean ± SD	P-value	Pairwise Significance		
					Group A vs Group B	Group A vs Group C	Group B vs Group C
Base line	128.15± 7.78	129.44± 7.93	131.47±7.54	0.21	0.77	0.18	0.53
1 st minute after extubation	131.82± 6.82	127.38± 8.52	127.18±6.71	0.01	0.04	0.03	0.99
3 rd minute after extubation	134.53± 7.02	126.15± 7.77	123.71±7.51	0.01	0.01	0.01	0.37
5 th minute after extubation	136.26 ±7.25	125.03± 7.21	122.21±8.53	0.01	0.01	0.01	0.28
10 th minute after extubation	137.59± 5.57	123.35± 5.02	120.79±7.94	0.01	0.01	0.01	0.22

N.B: SBP= Systolic blood pressure, mmHg= millimeter mercury , Group A= Control , Group B= Propofol 0.5mg/kg , Group C= Propofol 1mg/kg , SD= Standard deviation, n= number of patients, Vs= versus, P-value < 0.05 is statistically significant.

5.2.3 Comparison of diastolic blood pressure among groups

There were no significant difference among the groups in base line mean diastolic blood pressure (P =0.50). There were a significant difference of mean diastolic blood pressure between control (group A) and propofol groups (group B, and C) at 1st, 3rd, 5th and 10 minutes after extubation (P= 0.01). However there was no significant difference of mean diastolic blood pressure between propofol 0.5mg/kg (group B) and 1mg/kg (group C) at 1st, 3rd, 5th and 10 minutes after extubation (P> 0.05). (Figure 1)

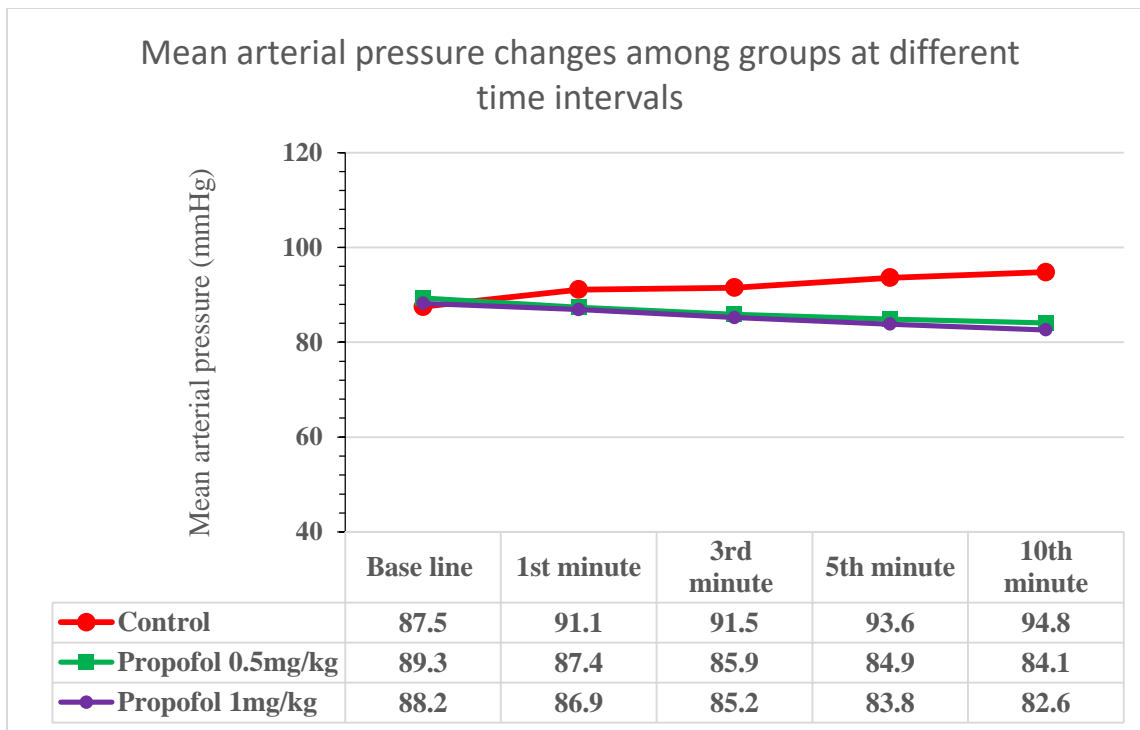
Figure 1. Comparison of mean diastolic blood pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.



5.2.4 Comparison of mean arterial pressure among groups

There were no significant difference among the groups in base line mean arterial pressure ($P=0.39$). There were a significant difference of mean arterial pressure between control (group A) and propofol groups (group B, and C) at 1st, 3rd, 5th and 10 minutes after extubation ($P=0.01$), however there were no significant difference of mean arterial pressure between propofol 0.5mg/kg (group B) and 1mg/kg (group C) at 1st, 3rd, 5th and 10 minutes after extubation ($P>0.05$). (Figure 2)

Figure 2. Comparison of mean arterial pressure among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.



5.2.4 Comparison of cough response during extubation among groups

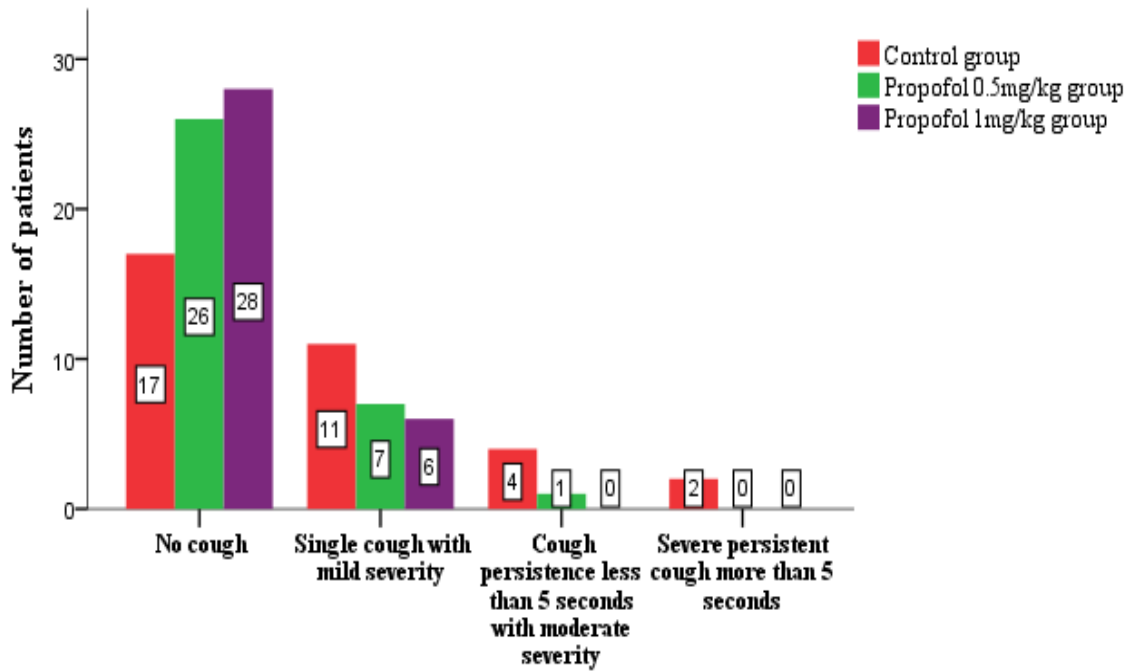
There were a significant difference on the occurrence of no cough between control (group A) and propofol groups (group B and C) ($P=0.01$). However there were no significant difference on the occurrence of no cough between propofol 0.5mg/kg (group B) and 1mg/kg (group C) after extubation ($P=0.80$).

The occurrence of no cough during extubation were significantly lower in propofol groups; 0.5mg/kg (group B) and 1mg/kg (group C) as compared to control (group A).

Grade (0) occurrences was shown in 17 patients (50%) in group A , 26 patients (76.5%) in group B and 28 patients (82.4%) in group C with P value = 0.01. Grade (1) occurrences was shown in 11 patients (32.4%) in group A, 7 patients (20.6%) in group B and 6 patients (17.6%) in group C with p value =0.33. Grade (2) occurrences was shown in 4 patients (11.8%) in group A, 1 patients (2.9%) in group B and none of patients (0.0%) in group C with p value =0.07 and Grade (3) occurrences was shown in 2 patients (5.9%) in group A and none of patients (0.0%) in group B and group C with p value =0.13 . (Figure 3)

Figure 3. Comparison of the occurrence and grade of cough during extubation among groups who underwent elective surgery at Jimma medical center from August 2022 to December 2022.

Graph depicts grade of cough during extubation among groups



CHAPTER SIX: DISCUSSION

The present study were conducted on 102 adult elective surgical patients under general anesthesia with endotracheal tube intubation who full fill the inclusion criteria and scheduled for elective general surgery. The demographic and clinical characteristics were comparable between the groups and statistically not significant ($P > 0.05$). At the end of surgery and following extubation at 1st, 3rd, 5th and 10 minutes there were significant difference on hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) between the groups ($P < 0.05$) and the occurrence and grade of cough following extubation were also different between the groups.

The present study confirmed that heart rate between groups were significantly different. There were no significant difference among the groups in mean baseline heart rate ($P = 0.30$) and there were a significant difference of heart rate between control and propofol 0.5 mg/kg and 1mg/kg groups at 1st, 3rd, 5th and 10 minute ($P = 0.01$) after extubation. However there were no statistically significant difference in heart rate between propofol 0.5mg/kg and 1mg/kg at 1st, 3rd, 5th and 10 minutes after extubation ($P > 0.05$).

The base line mean heart rate in control group was (93.71 ± 5.4), in propofol group 0.5mg/kg it was (92.41 ± 5.9) and in propofol 1mg/kg it was (94.62 ± 6.3). In control group there were an increment in heart rate up to 10 minutes after extubation compared to baseline value ($P = 0.01$). While in propofol 0.5mg/kg group there were a reduction in heart rate from 1 to 11 beat/minute and in propofol 1mg/kg there were a reduction in heart rate from 3 to 14 beat/minute over the base line mean heart rate value (92.41 ± 5.94 and 94.62 ± 6.34) respectively till 10 minutes after extubation which were statistically significant ($P = 0.01$).

In line with the current study a study done by Nagrale M.H *et al* 2016, Konda Sunil kumar *et al* 2018 and Ephrem Nigusse *et al* 2022 demonstrated that a reduction in heart rate in patients who received intravenous propofol 0.5mg/kg when compared with control group till 10 minute after extubation ($P<0.05$) (Nagrale, Indurkar and Pardhi, 2016; State, Author and State, 2018; Nigussie *et al.*, 2021). Another study done by Sarabjit Kaur *et al* 2006 and Yong-Chong Cheng *et al* 2011 also demonstrated that administration of propofol 1mg/kg and 1.5mg/kg respectively prior to endotracheal extubation results in a fall of heart rate which was statistically significant comparing to their control groups (Kaur *et al.*, 2006; Cheng *et al.*, 2011).

In contradict to the current result a study done by Soon Yong Jung *et al* 2014 and Amira A. Shaban *et al* 2016 concluded that patients who received propofol 0.3mg/kg and 0.8m/kg respectively didn't experience a reduction in heart rate up to 5 and 10minutes after extubation when compared to their control groups ($P>0.05$) (Jung, Park and Kim, 2014; Shaban, 2015) .The contradiction might be due to dosage difference of the study drug.

The present result demonstrated that there were a significant difference in systolic blood pressure between the groups. There were no significant difference among the groups in base line mean systolic blood pressure ($P =0.21$) and there were a significant difference of systolic blood pressure between control and propofol 0.5mg/kg and 1mg/kg groups at 1st, 3rd, 5th and 10 minutes after extubation ($P=0.01$), however there were no significant difference of systolic blood pressure between propofol 0.5mg/kg and 1mg/kg at 1st, 3rd, 5th and 10 minutes after extubation ($P>0.05$).

The base line mean systolic blood pressure in control group was (128.15±7.78 mmHg), in propofol 0.5mg/kg group it was (129.44±7.93 mmHg) and in propofol 1mg/kg it was (131.47±7.54 mmHg). In control group there was an increment in systolic blood pressure up to 10 minutes after extubation comparing to baseline value ($P= 0.01$). While in propofol 0.5mg/kg group there was a fall in systolic blood pressure from 2 to 6 mmHg and in propofol 1mg/kg there were a fall in systolic blood pressure from 4 to 10 mmHg over the base line mean systolic blood pressure value (129.44mmHg±7.93 and 131.47±7.54 mmHg) respectively till 10 minutes after extubation which was statistically significant ($P=0.01$).

In line with the current finding a study done by Konda Sunil Kumar et al 2018, Nagale M.H et al 2016 and Ephrem Nigusse et al 2022 demonstrated that patients who received 0.5 mg/kg propofol were shown a significant decrease in systolic blood pressure up to 10 minute after extubation compared to their control and comparison groups ($P < 0.05$) (Nagrle, Indurkar and Pardhi, 2016; State, Author and State, 2018; Nigussie *et al.*, 2021). A study conducted by Amira A. Shaban et al 2016 Sarabjit Kaur et al 2006 and Yong- Chong Cheng et al 2011 with propofol dose 0.8mg/kg, 1mg/kg and 1.5mg/kg respectively demonstrated that administration of those doses of propofol were shown a significant decrease in systolic blood pressure up to 10 minutes after extubation compared to their control and comparison groups ($P < 0.05$) (Kaur *et al.*, 2006; Cheng *et al.*, 2011; Shaban, 2015).

Contrary to the current finding Soon Yong Jung 2014 and his colleague concluded that no significant changes seen in systolic blood in patients who received propofol 0.3mg/kg. This might be due to lower dose of the study drug (Jung, Park and Kim, 2014). Mohammed Taghy Moein Vaziri 2013 and his colleague reported that in patients who received propofol 0.5mg/kg systolic blood pressure didn't constantly decrease up to 10 minutes after extubation. The contradiction might be due to difference in study design and inclusion of surgical procedure which was different from the present study (Moein Vaziri *et al.*, 2013).

According to the present study there were a significant difference in diastolic blood pressure between groups. There were no significant difference between groups in base line mean diastolic blood pressure ($P = 0.50$) and there were a significant difference of mean diastolic blood pressure between control and propofol 0.5mg/kg and 1mg/kg groups at 1st, 3rd, 5th and 10 minutes after extubation. However there were no significant difference of mean diastolic blood pressure between propofol 0.5mg/kg and 1mg/kg groups at 1st, 3rd, 5th and 10 minutes after extubation.

The base line mean diastolic blood pressure in control group was (87.65±5.11mmHg), in propofol 0.5mg/kg group it was (88.41±7.37 mmHg) and in propofol 1mg/kg it was (89.47±6.66 mmHg). In control group there was an increment in diastolic blood pressure up to 10 minutes after extubation comparing to baseline value (P= 0.01) and in propofol 0.5mg/kg there was a fall in diastolic blood pressure from 2 to 7 mmHg while in propofol 1mg/kg group there was a fall in diastolic blood pressure from 2 to 9 mmHg over the base line mean diastolic blood pressure value (88.41mmHg±7.37 and 89.47±6.66 mmHg) respectively till 10 minutes after extubation which were statistically significant (P= 0.01).

In line with the current result a study conducted by Nagale M.H et al 2016 Konda Sunil Kumar et al 2018, and Ephrem Nigusse et al 2022 reported that patients who received 0.5 mg/kg propofol were shown a significant decrease in diastolic blood pressure up to 10 minute after extubation compared to their control and comparison groups (P<0.05) (Nagrle, Indurkar and Pardhi, 2016; State, Author and State, 2018; Nigussie *et al.*, 2021). A study conducted by Amira A. Shaban et al 2016 and Yong- Chong Cheng et al 2011 reported that a propofol dose 0.8mg/kg and 1.5mg/kg respectively when administered prior to exubaion was shown a significant decrease in diastolic blood pressure up to 10 minutes after extubation compared to their control and comparison groups (P<0.05) (Cheng *et al.*, 2011; Shaban, 2015).

In contradict to the current result Soon Yong June 2014 and his colleague reported that there were no significant changes seen in diastolic blood pressure after extubation with the administration of propofol does 0.3mg/kg (Jung, Park and Kim, 2014). The contradiction might be due to use of low dose of propofol.

Mohammad Taghy Moein Vaziri et al 2016 reported that a propofol dose 0.5mg/kg results in a reduction of diastolic blood pressure at the time of drug administration (before extubation) but significant changes weren't seen after extubation ($P>0.05$). The contradiction might be due to difference in study design to the present study (Moein Vaziri *et al.*, 2013). A study done by Sarabjit Kaur et al 2006 also reported that no significant changes in diastolic blood pressure were seen up to 10 minutes after extubation ($P>0.05$) with administration of propofol dose 1mg/kg prior to extubation. The contradiction might be due to inclusion of different participant age group and surgical procedure which were different from the procedures included in the current study (Kaur *et al.*, 2006).

The present study confirmed that there were a significant difference in mean arterial pressure between the groups. There were no significant difference among the groups in base line mean arterial pressure ($P =0.39$) and there were a significant difference of mean arterial pressure between control and propofol 0.5mg/kg and 1mg/kg groups at 1st, 3rd, 5th and 10 minutes after extubation, however there were no significant difference in mean arterial pressure between propofol 0.5mg/kg and 1mg/kg at 1st, 3rd, 5th and 10 minutes after extubation ($P> 0.05$).

The base line mean arterial pressure in control group was (87.5 ± 5.11 mmHg), in propofol 0.5mg/kg group it was (89.26 ± 4.78 mmHg) and in propofol 1mg/kg group it was (88.24 ± 6.05 mmHg). In control group there was an increment in mean arterial pressure up to 10 minutes after extubation comparing to baseline value ($P= 0.01$). While in propofol 0.5mg/kg group there was a fall in mean arterial pressure from 1 to 5 mmHg and in propofol 1mg/kg group there were a fall in mean arterial pressure from 1 to 5.6 mmHg over the base line mean arterial pressure value ($89.26\text{mmHg}\pm 4.78$ and 88.24 ± 6.05 mmHg) respectively till 10 minutes after extubation which were statistically significant ($P=0.01$).

A study done by Nagale M.H et al 2016, Konda Sunil Kumar et al 2018 and Ephrem Nigussie et al 2022 demonstrated that patients who received 0.5 mg/kg propofol were shown a significant decrease in mean arterial pressure up to 10 minute after extubation compared to their control and comparison groups ($P<0.05$) (Nagrle, Indurkar and Pardhi, 2016; State, Author and State, 2018; Nigussie *et al.*, 2021), which supports the present study.

Another study conducted by Amira A. Shaban et al 2016 and Yong- Chong Cheng et al 2011 reported that a propofol dose 0.8mg/kg and 1.5mg/kg respectively when administered prior to extubation was shown a significant decrease in mean arterial pressure up to 10 minutes after extubation compared to their control and comparison groups ($P < 0.05$) (Cheng *et al.*, 2011; Shaban, 2015), which also supports the present study.

Contradict to the present study Soon Yong June et al 2014, Mohammad Taghy Moein Vaziril et al 2016 and Sarabjit Kaur et al 2006 reported that propofol dose of 0.3mg/kg, 0.5mg/kg and 1mg/kg respectively don't decrease mean arterial pressure up to ten minutes after extubation in comparison to their control groups (Kaur *et al.*, 2006; Moein Vaziri *et al.*, 2013; Jung, Park and Kim, 2014). The contradiction might be due to the use of small dose of the study drug, use of different study design and inclusion of different surgical procedure and study participant's age group compared to the present study respectively.

According to the present study there were a significant difference on cough response during extubation between groups. There were a significant difference on the occurrence of no cough between control and propofol 0.5mg/kg and 1mg/kg groups which were statistically significant ($P = 0.01$). However there were no significant difference on the occurrence of no cough between propofol 0.5mg/kg and 1mg/kg after extubation ($P = 0.85$).

The proportion of patients with no cough were 76.5% in propofol 0.5mg/kg, 82.4% in propofol 1mg/kg group and 50% in control group which were statistically significant ($P = 0.01$).

The proportion of patients with single cough were 20.6% in propofol 0.5mg/kg group, 17.6% in propofol 1mg/kg and 32.4% in control group ($P = 0.33$).

The proportion of patients with cough persistence, less than 5seconds were 2.9% in propofol 0.5mg/kg, none of patient's in propofol 1mg/kg and 11.8% in control group ($P = 0.07$). The proportion of patients with persistence cough more than 5 seconds were 5.9% in control group and none of patients in both propofol 0.5mg/kg and 1mg/kg groups ($P = 0.13$).

In line with the present study Soon Young and his colleague reported that the incidence of coughing during emergence was significantly lowered by propofol dose 0.3mg/kg compared to

their control group which was statistically significant ($P < 0.05$) (Jung, Park and Kim, 2014). Nagarale M.H and his colleague also reported that a propofol dose 0.5mg/kg was able to attenuate cough following extubation in approximately 90% of patients compared to their comparison group which was statistically significant ($P < 0.05$) (Nagrle, Indurkar and Pardhi, 2016).

Konda Sunil Kumar *et al* 2018 also reported that propofol dose 0.5mg/kg were able to attenuate cough and strain of extubation in $\geq 95\%$ of patients which were statistically significant ($P < 0.05$) (State, Author and State, 2018). Amira A. Shaban and his colleague demonstrated that the incidence and grade of coughing during emergence was significantly lowered by propofol dose 0.8mg/kg compared to their comparator group ($P < 0.05$) (Shaban, 2015).

Sarabjit Kaur and his colleague also demonstrated that propofol dose 1mg/kg when administered before oro-tracheal suction were able to reduce bucking on extubation which were statistically significant ($P < 0.05$) (Kaur *et al.*, 2006). Yong-Chong Cheng and his colleague reported that a cough caused by the stimulation of extubation were less by propofol 1.5mg/kg compared to their comparison group which was statistically significant ($P < 0.05$) (Cheng *et al.*, 2011).

In contradict to the present study Mohammad Tagay Moein Vazir and his colleagues demonstrated that propofol dose 0.5mg/kg reduces cough production at the time of drug administration (2 minute before extubation) but no significant difference was seen after extubation. The contradiction might be due to difference in study design and time of observation after extubation compared to the present study (Moein Vaziri *et al.*, 2013).

CHAPTER SEVEN: CONCLUSSION AND RECOMENDATION

7.1 Conclusion

Based on the present study it is concluded that there were a significant difference between control and propofol groups, however there were no significant difference between the two doses on attenuation of hemodynamic and cough response following extubation. Both intravenous propofol 0.5mg/kg and 1mg/kg when given prior to extubation were effective on attenuation of hemodynamic responses (heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure) to stimulation of extubation at 1st minutes, 3rd minutes, 5th minutes and 10 minutes after extubation.

7.2 Recommendations

Anesthetists might consider low dose propofol 0.5mg/kg for attenuation of hemodynamic and cough response to endotracheal extubation.

We recommend to do further study using RCT.

7.3 Limitation of the study

Discussion was limited due to inadequate literatures. The sample size enrolled in the present study was limited to adult patients and elective surgical procedures, hence it can't predict the hemodynamic and suppression effect of propofol during emergence in pediatric patients and ENT surgeries. So further investigations are needed on wider population with different age group and surgery type.

REFERENCES

- Asai, T., Koga, K. and Vaughan, R. S. (1998) 'Respiratory complications associated with tracheal intubation and extubation', *British Journal of Anaesthesia*, 80(6), pp. 767–775.
- Bindu, B. *et al.* (2013) 'A double blind, randomized, controlled trial to study the effect of dexmedetomidine on hemodynamic and recovery responses during tracheal extubation', *Journal of Anaesthesiology Clinical Pharmacology*, 29(2), pp. 162–168.
- Bostan, H. and Eroglu, A. (2012) 'Comparison of the Clinical Efficacies of Fentanyl, Esmolol and Lidocaine in Preventing the Hemodynamic Responses to Endotracheal Intubation and Extubation', *Journal of current surgery*, 2(1), pp. 24–28.
- Cheng, Y. C. *et al.* (2011) 'Effects of propofol versus urapidil on perioperative hemodynamics and intraocular pressure during anesthesia and extubation in ophthalmic patients', *International Journal of Ophthalmology*, 4(2), pp. 170–174.
- Cooper, R. M. and Khan, S. (2012) 'Extubation and Reintubation of the Difficult Airway', in *Benumof and Hagberg's Airway Management: Third Edition*, pp. 1018-1046.e7.
- Fuhrman, T. M. *et al.* (1992) 'Comparison of the Efficacy of Esmolol and Alfentanil to Attenuate the Hemodynamic Responses to Emergence and Extubation', *Journal of clinical Anesthesiology*, 4, pp. 444–447.
- Fujii, Y. *et al.* (1999) 'Combined diltiazem and lidocaine reduces cardio-vascular responses to tracheal extubation and anesthesia emergence in hypertensive patients', *Canadian Journal of Anesthesia*, 46(10), pp. 952–956.
- Gonzalez, R. M. *et al.* (1994) 'Prevention of endotracheal tube-induced coughing during emergence from general anesthesia', *Anesthesia and Analgesia*, 79(4), pp. 792–795.
- Hu, S. *et al.* (2019) 'Effects of intravenous infusion of lidocaine and dexmedetomidine on inhibiting cough during the tracheal extubation period after thyroid surgery', *Hu et al. BMC Anesthesiology*, 19(66), pp. 1–8.
- Jung, S. Y., Park, H. Bin and Kim, J. D. (2014) 'The effect of a subhypnotic dose of propofol for the prevention of coughing in adults during emergence from anesthesia with sevoflurane and remifentanyl', *Korean Journal of Anesthesiology*, 66(2), pp. 120–126.
- k.S savitha, D'souza Joylin Stephany, N. K. A. (2014) 'ATTENUATION OF HEMODYNAMIC RESPONSE TO EXTUBATION WITH I.V LIGNOCAINE', *Journal of Evolution of Medical and Dental Sciences*, 3(04), pp. 838–846.
- Kaur, S. *et al.* (2006) 'Role of propofol in prevention of extubation related complications in oral surgery', *Journal of Anaesthesiology Clinical Pharmacology*, 22(2), pp. 155–160.
- Khezri, M., Asefzadeh, S. and Kayalha, H. (2011) 'Comparison of intratracheal and intravenous lidocaine effects on bucking, cough and emergence time at the end of anesthesia', *Journal of Medical Science*, 27(4), pp. 793–796.
- Kim, E. S. and Bishop, M. J. (1998) 'Cough During Emergence from Isoflorane Anesthesia',

Anesthesia and Analgesia, 87, pp. 1170–4.

Kotani, Y. *et al.* (2008) ‘The experimental and clinical pharmacology of propofol, an anesthetic agent with neuroprotective properties’, *CNS Neuroscience and Therapeutics*, 14(2), pp. 95–106.

Kumar, L. M. *et al.* (2022) ‘Use of Effect Size in medical research: A brief primer on its why and how’, *Kerala Journal of Psychiatry*, 35(1), pp. 322–322. doi: 10.30834/kjp.35.1.2022.322.

Marik, P. (2005) ‘Propofol: Therapeutic Indications and Side-Effects’, *Current Pharmaceutical Design*, 10(29), pp. 3639–3649.

Miller, K. A., Harkin, Christopher P. and Bailey, P. L. (1995) ‘Postoperative Tracheal Extubation’, *Anesthesia and analgesia*, 80(4), pp. 149–72.

Mitchell, V. *et al.* (2012) *Difficult Airway Society Guidelines for the management of tracheal extubation, Membership of the Difficult Airway Society Extubation Guidelines Group.*

Moein Vaziri, M. T. *et al.* (2013) ‘Attenuation of cardiovascular responses and upper airway events to tracheal extubation by low dose propofol’, *Iranian Red Crescent Medical Journal*, 15(4), pp. 298–301.

Nagrle, M. H., Indurkar, P. S. and Pardhi, C. S. (2016) ‘Comparative study on Haemodynamic response to extubation : Attenuation with Lignocaine , Esmolol , Propofol’, *International Journal of Research in Medical Sciences*, 4(1), pp. 144–151.

Nigussie, E. *et al.* (2021) ‘Lidocaine versus propofol administration on the attenuation of hemodynamic responses during extubation in the adult elective surgical patient: A prospective cohort’, *Heliyon*. Elsevier Ltd, 7(8), p. e07737.

Nishina, K. *et al.* (1995) ‘Attenuation of Cardiovascular Responses to Tracheal Extubation with Diltiazem’, *Anesthesia and Analgesia*, 80, pp. 1217–22.

Salim, B. *et al.* (2019) ‘Effect of Pharmacological Agents Administered for Attenuating the Extubation Response on the Quality of Extubation: A Systematic Review’, *Cureus*, 11(12), pp. 1–17.

Shaban, A. A. (2015) ‘Effect of small dose propofol or midazolam to prevent laryngospasm and coughing following oropharyngeal surgeries : Randomized controlled trial’, *Egyptian Journal of Anaesthesia*. Elsevier B.V., 32(1), pp. 13–19.

State, T., Author, C. and State, T. (2018) ‘Attenuation of Cardiovascular Responses to Tracheal Extubation : Esmolol versus Propofol’, *Journal of medical science and clinical research*, 06(01), pp. 32292–32298.

Wong, T. H., Weber, G. and Abramowicz, A. E. (2021) ‘Smooth Extubation and Smooth Emergence Techniques: A Narrative Review’, *Anesthesiology Research and Practice*, 2021, pp. 1–10.

Annex I: Consent form and questionnaire

1. Consent from

Jimma university institute of health faculty of medicine department of anesthesia Questionnaire prepared to compare the effects of two different dose of propofol on attenuation of hemodynamic response during 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. 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: +251910844683

Email: melkamfikir511@gmail.com

Thank you!

2. Questionnaire for data collection

Data collection tool for institutional based comparative cross sectional study to be done on comparison effect of two different doses of propofol on attenuation of hemodynamic and cough response to tracheal extubation in adult elective surgical patients at Jimma Medical Center.

Date of data collection -----

Patient’s card no. -----

Data collector name and profession-----

Signature of data collector -----

1. Question about patient’s socio-demographic characteristic’s

S. N	Question	Response	Code
1	Age in year		
2	Sex	A) Female B) Male	
3	Weight in kg	-----	
4	Height in cm	-----	
5	BMI	-----	

2. Questions about anesthetics and surgical characteristics of patient’s

S.N	Question	Response	Code
1	ASA physical status	A. ASA I C. ASA III B. ASA II D. ASA IV	
2	Mallampatti classification	A. Class I C. Class III B. Class II D. Class IV	
3	Diagnosis	-----	
4	Type of surgery done	-----	
5	Type of induction agent used	Thiopental -----mg Ketamine -----mg Diazepam -----mg Suxamethonium-----mg	

		Vecuronium -----mg Pancuronium-----mg Halothane----- MAC %	
6	Number of trail to intubate the patient	A. First trail C. Third trials B. Second trail	
7	Intraoperative opioid used	A. Yes B. NO	If no skip to no..9
8	If yes specify type and dose	-----mg	
10	Duration of surgery (hr)	-----	
11	Duration of anesthesia	-----	
12	Study agent administered before extubation	A. Propofol (mg/kg) ----- B. Nothing -----	

3. Questions about patient's hemodynamic parameters

code	Extubation time duration	Hemodynamic parameters			
		HR	SBP	DBP	MAP
	Base line				
	1 - minute after extubation				
	3- minute after extubation				
	5- minute after extubation				
	10 – minute after extubation				

4. Questions about cough response during extubation

S.N	Question	Response	Code
1	Number of cough during extubation	A. No cough B. Single cough C. Cough persistence < 5 seconds D. Sustained cough more than 5 seconds	