ADDIS ABABA UNIVERSITY

COLLEGE OF HEALTH SCIENCE SCHOOL OF MEDICINE

DEPARTMENT OF ANESTHESIA

Effect of Priming Principle on the Induction Dose Requirement of Propofol, And Its Effect on Hemodynamic Parameter and Pain At Injection Site in Patient Undergoing Electives Surgeries Under General Anesthesia Public Hospital Addis Ababa Ethiopia From February 1 To April 30, 2022/2023,A Prospective Cohort Study.

INVESTIGATOR: GEBEREHANA GEBRE

ADVISORS:

1: **Mr. SULAIMAN JEMAL (MS**

2: **SILESHI ABiY (ASSISTANT PROFESSOR IN ANESTHESIA)**

Thesis submitted to the department of anesthesia, college of health sciences, Addis Ababa University, for the partial fulfillment of the requirement of a master degree in clinical anesthesia.

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NAME OF INVESTIGATOR	GEBEREHANA GEBRE (BSC IN ANSTHESIA). FAST 198826GMAIL@.COM.
NAME OF ADVISOR(S)	1.SULAIMAN JEMAL (BSC,MSC LECTURER IN ANESTHESIA) SULAIMAN JEMAL@AAU.EDU.ET). 2. SILESHI ABIY (BSC, MSC, ASSISTANT PROFESSOR IN ANESTHESIA.
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TOTAL COST OF THE PROJECT	35190BIRRR
ADDRESS OF INVESTIGATOR	+251 0996864354 FAST198826@GMAIL.COM

DECLARATION:

I understand and, declare that this thesis is my original work in partial fulfillment of the Master of Science in Anesthesia .I understand that plagiarism will not be tolerated and all directly quote material has been appropriately referenced.

Student name:

Geberehanagebre

Date _____ Signature _____

Submission to 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 Master of Science degree in Anesthesia.

Name of approval advisors	Date	Signature
1._____		_____
2._____		

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ABBREVIATION AND ACRONYM

ACP - Anesthesia Care Professional

A S A - American Society of Anesthesiologists

BMI - Body mass index

BSc - Bachelor of Sciences

BIS - Bi Spectral Index

BP – Blood Pressure

DBP – Diastolic Blood Pressure

ED50 – Effective dose in 50%

ECM - Effectives Concentration

GAB – Gamma Amino butyric Acid

HCP - Health Care Provider

HR – Heart Rate

ICU - Intensive Care Unit

IV – Intravenous

LCT – Long Chain Triglycerides

LOER - loss of Eyelid Reflex

Kg – Kilogram

MBP – Mean Blood Pressure

MD – medical Doctor

Mg/kg – Milligram per Kilogram

Min – Minutes

MmHg – Millimeters of Mercury

Ml – Milliliter

NDMR – Non Depolarizing Muscle Relaxant

NMDA – N-methyl-D-aspartate

PON - postoperative nausea vomiting

PIS – Propofol Infusion Syndrome

SBP – Systolic Blood Pressure

SD - standard deviation

SPSS - Statistical Package for Social Sciences

TIVA - Total Intravenous Anesthesia

ABSTRACT

Background: Priming techniques often referred to as auto co-induction is the procedure of delivering a pre-calculated amount of an induction agent prior to administering the full dose of the same agent.

The process of inducing of anesthesia is regarded as among the greatest significant instances in the administration of IV agent because it has been linked with a wide range of hemodynamic variations. Several induction agents have been used to induce anesthesia, with propofol gaining popularity due to its pharmacokinetic profile, but its primary drawback was its wide hemodynamic variability, which was mostly dose dependent.

In order to preserve the hemodynamic balance during propofol induction, different strategies were used. including concurrent use of N2O, administration of opioids, administration of sedative, and the use of benzodiazepines such as Midazolam, the addition of local anesthetics or magnesium sulphate, and the application of the priming principle).

Objective

To assess of Priming Principle on the Induction Dose Requirement of Propofol, And It's Effect on Hemodynamic Parameter ,and Pain at Injection Site in Patient Undergoing Electives Surgeries under General Anesthesia Public Hospital Addis Ababa Ethiopia from February 1 To April 30, 2022/2023.

Methodology

Prospective cohort study design were conducted among 88 Patient ASA I & II. We utilized the formula for sample size calculation with continuous results for two independent samples. Systematic random sampling technique was used. The investigation involved 88 patients who had been scheduled underwent elective surgery and were assigned to two equal groups. Group I received 0.6 mg/kg IV of propofol (25%, of the pre-calculated induction dose) while group II induced with routine technique. 30, second later, all two groups received IV induction with reaming propofol until loss of verbal response and eye lash reflex was attained. Hemodynamic Parameter were recorded at 0 (baseline), immediately 5, 10, minutes intraoperative in both group I and group II. We rate the severity of the pain during intravenous induction using the numeric evaluation scale. SPSS version 26 used for analysis. Shapiro wilk test and histogram t was

performed to determine whether the outcome dispersion were regular, followed by independent t-tests for normative data, Mann-Whitney U-tests for nonparametric data, and chi-square tests for categorical data. The level of statistical significance for all tests taken as $P < 0.05$**.**

Results

It was shown that the induction dose needed was reduced by 8% in priming group with p value of 0.001. The primed category's systolic, diastolic, and mean arterial blood pressures were steadier because their total propofol dosage was lower. Incidence of pain on injection of propofol in group I and group II was 63.6% and 90.6% respectively. Less pain had been attributed to priming.

Conclusions and recommendation:

An application of 25% (0,6mg/kg) of the induction dose of propofol associated mean reduction propofol dose by 8 %and improved hemodynamic stability. Propofol priming also associated with a considerably decreased incidence of pain.

CHAPTER: ONE

1. Introduction

Priming technique, often referred to as auto co-induction, is the procedure of delivering a pre-calculated amount of an induction agent prior to administering the full dose of the same agent. Its use with non-depolarizing muscle relaxants (NDMR) is well documented; a small priming dose, equivalent to 10–20% of the calculated dose of NDMR, given a few minutes before the intubating dose results in a rapid onset of neuromuscular blockade, improved intubating conditions, and a need for less medication.This was attributable to NDMR binding to the spare receptors following the administration of a priming dosage. To assess if the priming strategy reduces the effective dose of the induction drug and positively affects the pre intubation hemodynamic. [1].

With regard to induction drugs, this strategy tries to make use of the sedative, anxiolytic, and amnesic effects at sub-hypnotic dosages of induction agents when administered a short time before induction [1, 3, and4].

General anesthesia can be started by intravenous injection or inhalation When opposed to inhalation, intravenous injection causes unconsciousness to begin more quickly (10–20 seconds). Among IV induction agents Propofol most popular IV anesthetic drug for induction and sedation. It is associated with pleasant sleep, rapid recovery [3].

However, pain at the site of injection remains an important problem since the first clinical trial in 1977[5]. Propofol has many of the properties of an ideal anesthetic induction drug and is popular because it rapidly and smoothly induces anesthesia without airway irritation and results in a rapid recovery with an infrequent incidence of early post-operative nausea vomiting. The most often used intravenous (IV) anesthetic medication today, particularly for short procedures, day surgeries, or when a laryngeal mask airway is required [6]. Propofol can be taken continuously, has a quick onset, uniform anesthetic induction, quick recovery, and minimal

organ damage. Adults who are mechanically ventilated in critical care units can use it to sedate them and initiate the total intravenous approach (TIVA) [9].

But the main drawbacks of propofol are its costly price, the painful injections it causes, and the significant drop in systemic arterial blood pressure that results after its induction. It appears that both vasodilation and myocardial depression are responsible for the drop in systemic pressure that occurs after induction. Because sympathetic activity is decreased and intracellular smooth muscle calcium mobilization [9, 12].is directly impacted, propofol has a vasodilator effect. It appears that plasma concentration and dose affect both myocardial depression and vasodilation [3]. This study assessed if the priming strategy lowers the effective dose of the induction drug and positively affects the pre intubation hemodynamic.

1.1 STATEMENT OF PROBLEM

One of the main draw backs of induction with propofol is hemodynamic instability, which might show as hypotension or a decrease in systemic arterial pressure. If hypotension is not properly managed, it can cause many problems, including, decompensated shock, cardiac ischemia, renal failure, and even death[3,6].propofol cause hypotension which is the major problem in surgical patient that result in hypo perfusion to vital organ like brain kidney which result in delayed awkening,nausea and vomiting ,increased ICU stay, long hospitalization ,delayed wound healing, increased need of mechanical ventilation,incresed over all morbidity and mortality, patient discomfort[5]. in addition propofol induction is associated with pain during injection .This pain have a lot of impact on patient physiology like increased in heart rate, increased in blood pressure, which again result in cardiac ischemia, poor wound healing, decreased early mobilization ,decreased gastric movement,decerased coughing and expectoration which associate with hypoxia, pneumonia[6] .

In order to preserve the hemodynamic balance during propofol induction, different strategies were used, including, concurrent use of N2O, administration of opioids, and administration of sedatives. The use of benzodiazepines such as Midazolam, the addition of local anesthetics or magnesium sulphate, and the application of the priming principle [7].

But all are their own draw back. Therefore, this study aimed to assess the effect of priming principle on propofol mean induction dose and propofol induce hypotension, and propofol injection pain.

One study show that 60% of adult patients scheduled for vascular surgery experienced post-induction hypotension. This study found that post-induction hypotension was associated with higher mortality rates (8.8% against 5.2%), an extended stay in the intensive care unit (7.9% compared 2.0% no-hypotension), and a larger need for postoperative mechanical support (20.7% versus 3.8% no-hypotension) in patients [5].

Because of reduced contraction of the heart, peripheral blood vessel resistance, and autonomic tone, propofol induction at a dose of 2 to 2.5 mg/kg causes a 25 to 40% reduction in blood pressure. Because of the heart-slowing effects of propofol, people may experience severe bradycardia, cardiac arrest, or total atrioventricular block [2].

It has been found that intraoperative hemodynamic alterations are significant prognostic indicators of morbidity and mortality. Evidence demonstrates that general anesthesia-induced hypotension is linked to unfavorable Patient results following both cardiac and non-cardiac procedures. The chance of death is said to rise by more than 1% every minute for each mmHg drop in systolic blood pressure [4].

Post marketing research found that in 53% of patients systolic blood pressure drop by 15 to 35% after propofol was used to induce anesthesia. Bradycardia was also noted at the time of anesthesia induction in 2% of patients [9].

Propofol can also produce acute respiratory depression and pain following intravenous administration, which might make patients dissatisfied with the milky substance during induction(5).About 85 to 100 percent of people who receive a propofol administration report experiencing pain and 30% develop severe pain[6].

There are several ways to lower the amount of propofol needed for induction, including using it concurrently with nitrous oxide, opioids, barbiturates like thiopentone, and benzodiazepines like

midazolam, augmentation with local anesthetics or magnesium sulphate, and priming principle but all are associated with complication [7]. Priming principle was selected because of lack of complication associated with it

1.2. SIGNIFICANCE OF THE STUDY

Hemodynamic instability in surgical patients induced with propofol really a problem in all operation setting across the country. This is problem in all operation room of the country. Propofol induced Hemodynamic instability is our day to day or problems or clinical experiences. Patient have the right to comfortable without minimum Hemodynamic instability but this is not possible by with propofol induction.

Different study was done in abroad with RCT but the not adequately calculate their sample size, they have not involve black race, and in addition non- genetic factor like temperature, patient emotion and psychology are not considered by previous study. Any treatment or medication or technique like priming when applied on patient should fit for the respective patient identities.

The major importance of this study when we compare from other study first it proved whether priming principle are functional or not in black race. different study was conducted on effect of genetics variants on propofol pharmacodynamics and pharmacokinetic and their finding show that vulnerability for propofol impacts significantly affected by individual variations in genetic variables like, single nucleotide polymorphisms in the genes encoding enzymes that regulate metabolism, biochemical transporters, and biochemical binding sites of propofol. Propofol sensitivity may be influenced by genetic variants in the genes for GABRA2, GABRB1, GABRG2, GAD1, andSLC1A3.

Secondly this study play as road map for researcher in the field to conduct study on different future of propofol because propofol most commonly used all and every aspect of this drug should be studded.

Thirdly this study is to determine whether priming propofol would decrease the overall induction dose of propofol and, consequently, the cost to the patient in our current economically depressed

environment. Now days most of surgical procedures which conducted under general anesthesia via endotrachealtube,laryngeal mask air way ,sedation with mask all are performed by using propofol. Currently all anesthesia professional preferred propofol for most clinical purpose as compared to other iv agent.in addition propofol is well known drug which used in ICU for sedation.to day ministry of health focused on day case surgery, near future most surgical procedure done under day care for such kind of day care procedure the most commonly used drug is propofol b/c of short half-life and fast recovery. Over all propofol preferred, important, and most commonly used drug, so using this drug wisely in economical way is mandatory.

The other most significance of this study is decreasing the incidence of complication like hypotension, apnea and pain. Previous study give hint that higher dose of propofol result in hypotension and collapse during induction which result in delayed awaking .also it is known that propofol cause pain during injection this is more with large and concentrated dose. Therefore, this study aimed to assess the effect of priming principle on propofol mean induction dose and propofol induce hypotension, and propofol injection pain.

CHAPTER: TWO

2. Literature Review

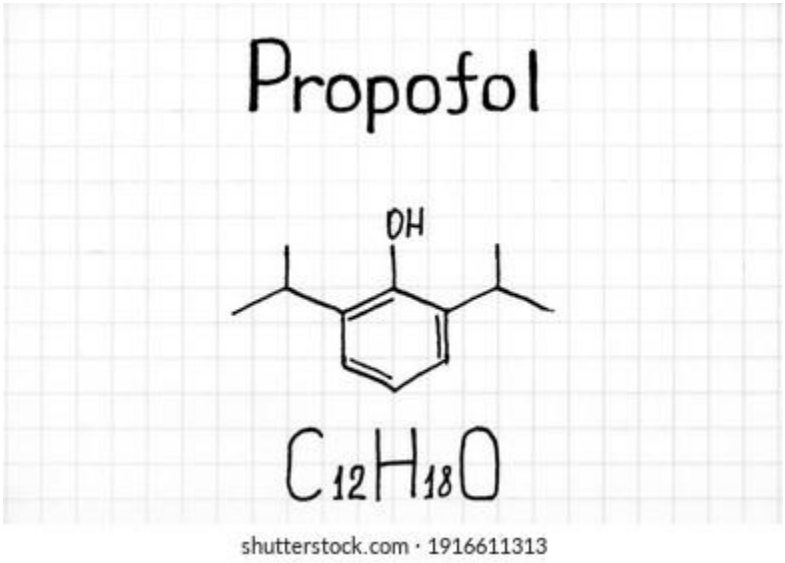
A. Regional anesthesia is currently recommended for surgeries; however, several surgeries require general anesthesia. Inhalation or intravenous injection may be used to start general anesthesia [11].

The research that produced propofol started in 1973 at Mackles field, England. Dr. R. Ronald Shark conducted the first clinical trials. Dr. Brain Kay and Dr. Gorges Rolly first used propofol in a clinical setting in 1977. Propofol, also known as 2, 6, di-isopropyl phenol, is made composed of a phenol ring with two isopropyl groups attached. 2, 6-diisopropylphenol's anesthetic characteristics were first noted in January 1973 by ICI (recorded as ICI 35868) in Cheshire, England. The first clinical trials with a 1% preparation prepared in Cremophor EL were carried out in Europe in 1977; however, this formulation was not clinically evaluated in the United States [5].

Due to its remarkable abilities to induce anesthesia quickly, smoothly, and with no lasting effects, propofol has become increasingly popular in recent years [9].

In recent decades, propofol has become a viable substitute for thiopentone. It has a number of benefits over thiopentone, including quicker awakening and orienting, improved intubation condition and upper airway integrity, and a reduction in post-operative nausea and vomiting [11] Propofol is used for sedation, target-controlled infusions, total intravenous anesthesia, and induction of anesthesia.

Propofol is present in DIPRIVAN® (propofol) Injectable Emulsion, a sterile, no pyrogenic emulsion that can be administered intravenously. Chemically known as 2, 6-diisopropylphenol, propofol has a molecular weight of 178.27. The formulas for the structures and molecules are:



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1; THE FORMULAS FOR THE STRUCTURES AND MOLECULES ARE: [45]

Propofol is made as an oil-in-water emulsion because it is only marginally soluble in water. The pH range of the DIPRIVAN Injectable Emulsion is 7–8.5 and it is isotonic [14].

The central nervous system depression caused by propofol is most likely mediated by -amino butyric acid (GABA) and glutamatergic N-methyl-D-aspartate (NMDA) receptor acting as agonist and antagonist, respectively(10). Propofol, in particular, as a GABA receptor anesthetic, modulates GABA action at GABAA receptors by either prolonging inhibitory postsynaptic currents mediated by GABAA receptors or by increasing GABA release via presynaptic mechanisms [11]. Anesthetics can attach to lipophilic pockets in various GABAA receptor subunits, increasing the chloride influx current and causing neuronal hyperpolarization[17].

Propofol causes the release of nitric oxide, acts as a calcium channel blocker, and stimulates protein kinase at the cellular level. As a result, clinically, propofol administration reduces cardiac output and arterial pressure. This cardiovascular negative chronotropic effect has been attributed in various ways to the drug's effects on peripheral resistance, inotropy, and heart rate (by reducing the baroreceptor response to decreased blood pressure). Propofol hemodynamic effects

may thus result from decreased ventricular preload or afterload, depression of cardiac contractility, and suppression of compensating tachycardia [13]

Following induction, there is a drop in systemic pressure that appears to be caused by both myocardial depression and vasodilation. Propofol vasodilator action is brought about by its direct impact on intracellular smooth muscle calcium mobilization and a decrease in sympathetic activity. There seems to be a dose- and plasma concentration-dependent relationship between myocardial depression and vasodilation [14]

Methods for reducing the amount of propofol required for induction, such as using it concurrently with other drugs such as nitrous oxide, opioids, barbiturates such as thiopentone, and benzodiazepines such as midazolam, augmentation with local anesthetics or magnesium sulphate, and the priming principle [15].

Study by [Ju-Mei N, Nian-Chih H.] shows that Pre-induction usage of 66% nitrous oxide in oxygen with 2 mg/kg of propofol decreased the induction dose of propofol by 44%, shortening the induction period without desaturation. The total amount of propofol used was greatly reduced by both nitrous oxide and dexmedetomidine. Therefore, both of these substances have the potential to be utilized as anesthetic adjuvants to lessen the side effects brought on by the infusion of propofol. Dexmedetomidine has the potential to be a safer and more effective substitute for nitrous oxide due to the absence of any known long-term or environmental negative effects [20]

The induction dose of propofol was discovered to be reduced by the additive action of propofol with fentanyl and alfentanil for the induction of anesthesia. In the study carried out [Ben-Shlomo I, Finger J,]where six different dosage combinations were studied only to determine the type of interaction during induction of anesthesia, it was discovered that 23% of the ED50 of fentanyl was required in conjunction with 75% of the ED50 for propofol to achieve the ED50 of the combination(Due to increased vagal activity, it has been discovered that combining opioids and propofol worsens the drug's respiratory depressive effects, sedation, and potentially deadly consequences such cardiac arrest[22].

The amount of(f propofol needed for tracheal intubation was greatly decreased when midazolam (0.2-0.5 mg kg1) and diazepam (0.3-0.5 mg kg1) were delivered intravenously after 2 mg/ kg of propofol[16,17]. Midazolam pre-treatment decreased the amount of propofol needed for induction in both younger and older patients, however neither the cardiovascular stability nor the incidence of apnea were shown to be improved [17]

Pre-medication with 0.6 mg of clonidine considerably reduced the need for propofol during surgery; however it was linked to longer recovery durations. When clonidine was administered, less propofol was necessary to produce the same BIS-defined state of anesthesia. The absence of any explicit intraoperative consciousness and the absence of any indications of implicit recollection suggest that the anesthesia brought on by clonidine and low-dose propofol may be comparable to the anesthesia brought on by a higher dose of propofol by itself. It is obvious that larger trials will be required to demonstrate definitively that a lower dose of propofol paired with clonidine is as safe as a higher dose propofol in preventing intraoperative awareness. Patients who received a combination of clonidine and propofol had mean heart rates that were more hemodynamic ally stable than patients who got fentanyl-propofol or just propofol, and these differences were statistically significant at the 3min, 5min, and 10min marks. When a patient receives a combination of the anesthetic medications propofol and clonidine before to surgery, their mean arterial pressure is initially raised. The Clonidine-Propofol group has lower Mean Arterial pressure during AMBU LMA insertion and subsequently from 1min, 3min, 5min, and 10min compared to the Fentanyl Propofol and Propofol solo groups; this difference is statistically significant at all-time intervals [18].

Combining thiopentone and propofol decreased the induction dose of propofol but also resulted in a prolonged recovery because of the synergistic effects of the two drugs [19].

In a dose-dependent way, lignocaine and bupivacaine dramatically improved the hypnotic effects of propofol. Lignocaine 3.0 mg /kgand bupivacaine 1.0 mg/ kg, the highest doses examined, respectively lowered the hypnotic dose of propofol by 34.4% and 39.6%. We come to the conclusion that the IV. Dose of propofol should be adjusted if lignocaine or bupivacaine are

administered into soft tissue prior to the induction of anesthesia by the former [46]. However, using local anesthetics with propofol did not relieve any pain and was accompanied with a significant drop in blood pressure; this was especially true of bupivacaine.

Magnesium sulfate and clonidine hasten the onset of anesthesia when propofol is used. Compared to the clonidine and control groups, the time for BIS to reach 60 was considerably shorter in groups M and CL (P 0.0001), but postoperative recovery was slower with magnesium sulphate. Heart rate and arterial blood pressure were no statistically significant variations across the groups. Magnesium and clonidine considerably reduced the amount of propofol needed to initiate and maintain anesthesia (P 0.0001) [47]

When propofol and ketamine were combined, hemodynamic stability increased, whereas the need for anesthesia decreased when propofol and magnesium sulphate were combined. When ketamine was used, side symptoms such nausea was found to be more common, but postoperative pain was shown to be more common when magnesium sulphate was used.

Prospective randomized controlled study included 100 individuals. Two groups of 50 patients each were randomly assigned to the patients. The control group got 2 mg/kg IV propofol until loss of eyelid reflex the study or priming group's mean induction dose was considerably lower. Only five minutes after introduction did the heart rate differ significantly. The study group consistently had considerably higher systolic, diastolic, and mean blood pressure. While fasciculation’s were more common in the priming group, apnea incidence was higher in the control group [21].they concluded that Propofol total induction dose can be decreased while simultaneously attenuating hypotension by efficiently utilizing the priming principle. The sole drawback was that suxamethonium induced fasciculation’s were more obvious.

Prospective, randomized, double-blind trial, 100 individuals were included. Patients in group B (Bolus Group) received intravenous injections of fentanyl g kg-1 over a period of 30 seconds, followed by intravenous infusions of propofol until loss of eyelid reflex (LOER). Patients in group P (Priming Group) received 25% of the calculated total dosage of Inj. Propofol 2 mL kg-1 30 seconds after receiving Inj. fentanyl g kg-1 over 30 seconds and once more after receiving Inj.

Propofol g kg-1 until LOER. Before induction, immediately after intubation, one minute after induction, and five minutes following intubation, various hemodynamic parameters were measured. Results: A dosage decrease of 28.92% was observed [22].

Randomized controlled trial at Operation theatre complex, Shalamar Hospital show that, 100 patients, ranging in age from 18 to 55, were split evenly between the control and research groups. Following routine anesthetic monitoring, both the Control (C) group and the Study (S) group received intravenous propofol for the traditional way of inducing general anesthesia and the Priming principle, respectively. In the study group (S), the mean induction dose of propofol was 70.90 +6.77 mg, while it was 94.60 +20.22 mg in the in non-exposed l group (C),and a p-value of 0.000. The mean discrepancy induction dose among the groups was 23.7 3.45 mg [23].

68 individuals in total (ASA I and II), aged 20 to 40, who were having elective general, orthopedic, or gynecological surgery were included in the double-blind prospective randomized research. All patients received fentanyl 1 mg kg-1 followed by either 0.3 mg kg-1 of ketamine (group KP), midazolam 0.03 mg kg-1 (group MP), propofol 0.4 mg kg-1 (group PP), or 3 ml of normal saline (group SP - control). The titrated dosage of propofol was used in conjunction with 2 ml of lignocaine to induce anesthesia. Groups KP, MP, and PP required considerably less propofol to induce anesthesia than the control group (1.2 mgkg-1, 1.4 mgkg-1, and 1.6 mgkg-1, respectively), using lack of reaction to verbal orders as the end point of induction (2.7 mgkg-1). Following induction, a decrease in mean arterial pressure (MAP) was seen in all the groups, ranging from a maximum of 21% in the control group to a minimum of 4% in group KP. All patients displayed relative bradycardia, but the KP group had the least of it. The MAP decreased by 13% and 11%, respectively, for the groups MP and PP. they draw the conclusion that all co-induction agents require less propofol than a placebo, and that the hemodynamic effects were dose-dependent. A reasonable and secure substitute for midazolam co-induction would seem to be ketamine. When compared to midazolam, propofol auto-co-induction has no advantages in terms of cardiovascular stability[44].

The clinical efficacy of propofol auto-co-induction, midazolam propofol co-induction, and a control group in terms of dose reduction and peril-intubation hemodynamics was compared. The study included 90 patients scheduled for upper abdominal surgery that was sorted into 1 of 3 equally sized categories at random. The first group received 0.5 mg/kg propofol IV (20% of the calculated induction dose), the second group received 0.05 mg/kg IV midazolam, and the third group received 3 ml of normal saline. This was followed by a 2-minute IV induction with propofol in all three groups at a predetermined rate until a spectral index of 45 was achieved. In comparison to the control group, the mean induction dose requirement was 45.37% lower in the midazolam co-induction group and 31.88% lower in the propofol auto-co-induction group(24)].

The study by included 100 ASA I and II patients of either gender between the ages of 18 and 55 who had appointments for general anesthesia-based show reduction of induction dose requirement by 27.48%, with negligible per intubation hemodynamic changes but a rising prevalence of post-suxamethonium fasciculation's[15].

Another study by [25] involves 75 patients with an ASA grade I are included in this prospective, observational, and non-interventional study. Participants' ages range from 20 to 50. Three groups of 25 patients each were formed from all of the patients. PP Group I, MP Group II, and Group III (P). Group I received 0.5 mg/kg propofol two minutes before the induction drug, while Group II received 0.05 mg/kg midazolam. Measurements were made of the propofol induction dosage and several hemodynamic parameters. When comparing Groups I and II to Group III, the induction dose of propofol in each group was 74.4 mg, 66.36 mg, and 136.4 mg, respectively. This variation was statistically noteworthy (p 0.05). In group I, which represents auto-co-induction, hemodynamic stability during the peril-intubation interval was better. And researcher conclude that Propofol auto-co-induction and midazolam co-induction both considerably lower the induction dose of propofol while improving hemodynamic stability during the pre-intubation period. The priming appears to be cost-effective because it greatly lowers the overall dose of propofol needed, and none of the groups experienced any notable negative intra- or postoperative consequences..

An observational study was conducted on 180 patients aged 20 to 57 years who were classified as ASA-I or ASA-II and were undergoing surgery that required general anesthesia as the mode of anesthesia of choice to determine the effect of the priming principle in relation to Propofol. The mean induction dose in group A (prming group) was 81.229.68, while it was 113.0212.63 in group B (control group). As a result, we saw a 25% reduction in induction dose requirement in group A[27].

Compared to administering propofol (2.5mg/kg) alone, ketopropofo (0.8mg/kg ketamine and 1 mg/kg propofol) plus 0.2mg/kg fentanyl provides a number of benefits. Stable hemodynamics, no respiratory depression, quick recovery, and effective postoperative analgesia. Therefore, they recommend intravenous ketofol as an induction medication, especially for patients having quick surgical procedures [25, 44].

According to the studies on the priming principle mentioned above, all are associated with a variety of side effects. The use of propofol results in the greatest dose reduction, with 66% nitrous oxide in oxygen and 2 mg/kg propofol lowering the induction dose by 48%. The next significant decrease is a study done by which is a 40% dose reduction. This may be due to all of the patients being premeditated with intravenous fentanyl and intravenous 20 mg lignocaine before propofol to reduce pain [20, 44].

The listed induction dose decrease in the above study done on the priming principle is 21%, which is assumed to be due to patients not being over premeditated. I also noticed that the maximum decreasement occurs in patients who are given total induction two minutes after priming and the minimum decreasement occurs in patients who are induced within two seconds of priming.

Another most problem of propofol induction is a decrease in arterial blood pressure during anesthesia induction. The study included 90 patients scheduled for upper abdominal surgery who was randomly assigned to 1 of 3 equal groups. The first group received 0.5 mg/kg propofol IV (20% of the calculated induction dose), the second group received 0.05 mg/kg IV midazolam, and the third group received 3 ml of normal saline. At the post-priming interval, the propofol

auto-co-induction group experienced a statistically significant (P0.001) decrease in HR. The HR increased after intubation in all three groups, but the propofol group experienced the least increase. The control group's mean SBP was found to be stable at induction, while the other two groups experienced a slight drop. The midazolam co-induction group had the greatest increase in SBP after intubation (20.19%).At induction, mean DBP was observed to be maintained in the control group (with a slight fall observed in other two groups). The propofol auto-co-induction group had the greatest drop in DBP (17.99%) from the pre-induction value at the post-induction interval. The midazolam auto-co-induction group had the greatest increase in DBP (16.80%) from baseline at the post-intubation interval [28].

In one randomized, double-blind trial, 100 individuals were included. Patients in group P (Priming Group) received 25% of the calculated total dosage o propofol. Patients in group B (Bolus Group) received intravenous injections of fentanyl g kg-1 over a period of 30 seconds, followed by intravenous infusions of propofol until loss of eyelid reflex (LOER Inj. Propofol 2 mL kg-1 30 seconds after receiving Inj. fentanyl g kg-1 over 30 seconds, and once more after receiving In .Group B had significantly lower systolic blood pressure (11.82%) one minute after induction, immediately after intubation (11.36%), and 5 minutes after induction (6.91%) than group P. Similarly, group B had significantly lower diastolic blood pressure and mean arterial pressure values one minute after induction (5.35%, 8.2%), immediately after intubation (3.99%, 7.23%), and five minutes after induction (2.2%, 4.27%) than group P[22].

From the above study on priming principle I noted that small decrement in primed group than control group This is most likely due to the fact that less propofol was used in primed.

According to the literature reviews above, various techniques have been investigated to reduce the total induction dose requirement of propofol as well as its associated hemodynamic instability, with some encouraging results. Pain reduction during administration was also investigated, with varying degrees of success recorded. There are, however, very few reports on the priming principle's application to the induction dose requirement.

Pain during propofol injection is one of the problem propofol injections. In adults, the incidence of pain during anesthesia induction ranges from 28% to 90% and can be severe. The prevalence of pain in children ranges from 28% to 85% [29]. The incidence and severity of propofol injection pain increases with age. This could be due to children's smaller veins. There is no difference in the occurrence of propofol injection pain between men and women. When compared to other intravenous anesthetic agents, propofol has a high incidence of pain on injection. Pain is frequently described as severe or even intolerable. The high incidence of pain on injection is a clinically relevant disadvantage, particularly with traditional LCT formulas, and has been ranked as the seventh most important clinical problem of modern anesthesia by anesthesiologists[33].

The cause of pain after propofol injection is unknown, but several mechanisms have been proposed[34].

Clement and Arndt proposed that pain on injection of some anesthetic agents is caused by the physiological osmolality or pH of their formulations. They discovered that pain occurred at 1 osmol/kg during infusion and 3.0 osmol/kg during rapid injection. At pH values less than 4 and greater than 11, acidic and alkaline solutions cause pain, respectively. They also discovered that increasing osmolality, acidity, and alkalinity reduced pain latency. The osmolar concentration and pH of the solutions that came into contact with the intima of a superficial hand vein were both factors in the pain production. The amount injected and the flow of blood through the vein also affected the level of pain. They also proposed that the painful sensation from veins is most likely caused by neural elements within the vein walls, such as free afferent nerve endings between the media and intima[35].

.Propofol, on the other hand, is nearly isotonic, nonhyperosmolar, and has a pH between 6 and 8.5. As a result, this theory cannot account for the pain caused by a propofol injection[36].

Certain factors, according to[37]., are important in the causation of pain after propofol injection. They found that when propofol was injected into a large vein in the antecubital fossa, it did not cause pain. This is presumably because the drug is injected into the midstream of blood flow in

the vein lumen, resulting in minimal contact with the sensitive wall at high concentration. Furthermore, the drug may be effectively buffered by blood, with which it can freely mix. Another important consideration is the length of time the vein wall is exposed to the propofol injection. They found that a slow propofol injection caused more pain than a rapid bolus. Perhaps a quick bolus of the drug is removed from the vein and replaced with blood. They also observed a species difference in propofol injection pain. They hypothesized that the pain was caused by an indirect irritant effect, rather than a direct irritant effect.

Furthermore, when the active component of the propofol emulsion comes into contact with vascular endothelium, it causes the release of mediators from the kinin cascade, such as kininogen, resulting in pain stimulation. This results in a slightly delayed sensation of pain as opposed to the immediate sensation of pain caused by a direct effect [29].

As propofol has an almost physiological osmolality and pH (0.303 osmol.kg1; pH 8.0), it is suggested that the pain is related to the concentration of propofol in the aqueous phase and not to] the formulation. They discovered that the intensity of pain increased with the concentration of propofol and was always greater with glucose as the diluent than with intralipid. Pain on injection was reduced by lowering the propofol concentration in the aqueous phase with intralipid they observed that the intensity of pain increased with the concentration of propofol and was always greater with glucose as the diluent than with intralipid. Pain on injection was reduced by lowering the propofol concentration in the aqueous phase with intralipid.[35].

[33, 34, 35] proposed that propofol concentration in the aqueous phase could be an important variable in pain associated with propofol injection. They discovered that the propofol concentration in the aqueous phase of Diprivan is relatively high (18.57 mg.ml1), indicating that the active component is not completely dissolved in the lipid vehicle. The drug will be distributed differently between the two phases in the propofol emulsion preparation, with an outer aqueous phase and an inner lipid phase. Only the outer aqueous phase of a bolus injection comes into contact with the vein's intima. The presence of an irritating agent in the aqueous phase may be the cause of venous pain during administration. Propofol, like all phenols, causes

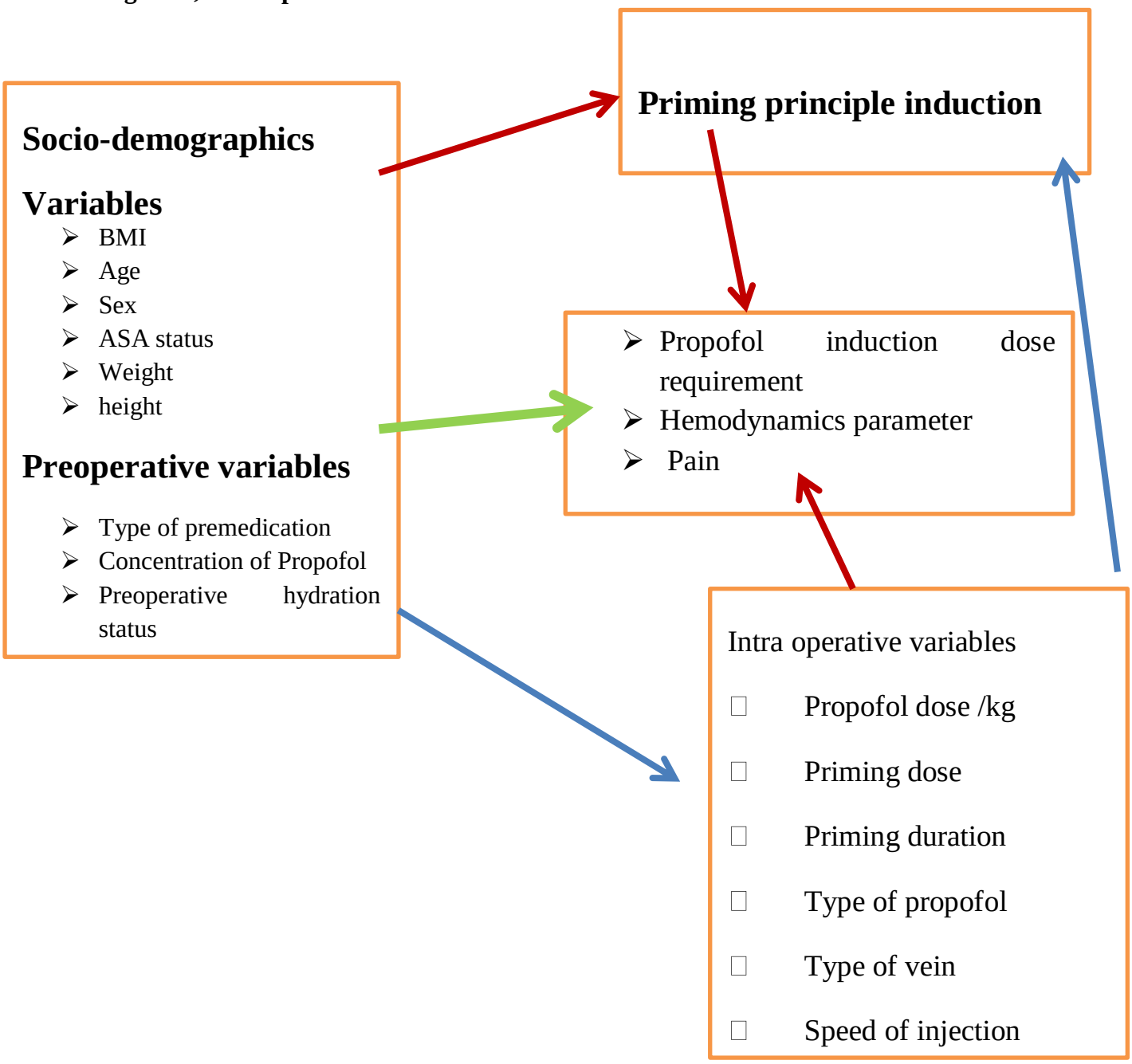
skin and mucous membrane irritation. As a result, bolus injections of propofol preparations are likely to cause pain.

Several methods for pain prevention have been tried with varying degrees of success based on the proposed mechanisms and factors associated with propofol injection pain. The results of published studies have varied, owing to differences in methodology.

In a double blinded prospective clinical trial involving 77 patients Liljeroth et al wanted to see if the intensity of pain on injection of propofol could be reduced by previous slow administration of a low dose propofol via the same intravenous route, and they found that the maximal intensity of local pain induced by the main dose of propofol was lower 2 minutes after a 0.5ml priming dose of propofol than the control, indicating that a priming dose of 5mg was effective in reducing the pain felt on induction of propofol[35]. This observation was supported by Anil et a1, who observed a lower number of patients (2%) with decreased pain after priming with 20% of the total induction dose compared to 34% of patients in the e control group who felt pain. Similarly, after priming with 0.4mg/kg propofol, fewer patients (16%) felt pain compared to the control (22%) in a clinical trial conducted by Djaiani and Ribes[40]. As a result, it is hoped that this study will be able to create a local data base for propofol research while also assessing its effect on hemodynamics, and pain, as this will add to the body of knowledge about propofol.

2.1. CONCEPTUAL FRAME WORK

Figure 2; 2conceptual frame work



2.2. RESERCH HYPOTHESIS

1 .H0: There is no difference in mean induction dose requirement in exposed and non- exposed group.

HA: there is difference in mean induction dose requirement in exposed and non- exposed group.

2. H0: There is no difference in hemodynamic parameters in exposed and non- exposed group.

HA: there is difference in hemodynamic parameters in exposed and non- exposed group

3. HO: there is no difference in injection pain in exposed and non- exposed group.

HA: there is difference in injection pain in exposed and non- exposed group.

CHAPTERL: THREE

3. Objective

3.1. General objective:

To assess the effect Of Priming Principle of propofol on the Iduction Dose Requirement of Propofol, and It's Effect On Hemodynamic Parameter and Pain At Injection Site In Patient Undergoing Electives Surgeries Under General Anesthesia Public Hospital Addis Ababa Ethiopia From February 1 To April 30, 2022/2023, A Prospective Cohort Study.

3.2. Specific Objectives:

- To compare mean induction dose between exposed group and non-exposed group.
- To compare mean hemodynamic parameter between exposed group and non-exposed group.
- To assess the effect of priming dose of propofol on the induction pain of propofol.

CHAPTER: FOUR

4. Methodology

4.1. Study area

This study was conducted in Addis Ababa, the capital city of Ethiopia. The city is located on an average altitude of two thousand fifty meters over sea level and has a climate that is subtropical for the area. There are 11 sub-cities in the city, which has a total area of 520 km2. The majority of the nation's ethnic groupings are represented. It contains 86 health clinics and 14 public/government hospitals. From this, by adopting a lottery system, the Black Lion Specialized, zewditu, petres referral Hospitals were chosen as the research area. Study was carried out in three public hospitals.

Zewditu Memorial Hospital is a government hospital located in kirkos sub city wereda 08, Addis Ababa, Ethiopia. The hospital was constructed by a non-governmental institution before becoming open to the general public in 1976E.Ccurrently the hospital is directed by the addis Abba health Brue Ministry of Health. Currently have 200 beds in total, 46 of which are in the obstetrics, gynecology, and postnatal department.

Tikur Anbessa specialized hospital, Ethiopia's largest hospital, multispecialty tertiary care teaching hospital was established in 1972 and was given to the FMOH in 1998 when it changed its name to university teaching hospital. Ethiopia's largest referral hospital is TASH. With 14 operating rooms (OR), it provides diagnostic and treatment for about 370,000–400,000 patients yearly. It also performs close to 8000 surgeries. The hospital offers a variety of reproductive health services, including gynecologic and obstetric care. On average 25 new born delivered each day in the hospital. The hospital has one operation theatre dedicated only for cesarean section with additional emergency OR. 8to 10 caesarean sections are performed on average every day at the hospital, of which one third are planned operations. St. Peter’s Specialized Hospital was established in 1953 E.C.now run under Ministry of Health. Have objectives of to improve research, training and health service. Have been six operation suites.

4.2. Study design and period

Institutional-based prospective cohort study was carried out in public hospitals of Addis Ababa, From February 1 To April 30/2022/23.

4.3. Population

4.3.1. Source of population

All surgical patients undergoing surgery at chosen public hospitals in Addis Ababa who had general anesthesia by endotracheal intubation with propofol were a source population.

4.3.2. Study population

Adult patients who were undergo elective surgical procedures via endotracheal intubation in both sex who where induced by propofol between the ages of 18 – 65years in selected public hospitals in Addis Ababa across the research durations that satisfy the eligibility requirements.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

ASA class I and II patients between the ages of 18– 65years of both sexes, Normotensive patients, who were undergo elective surgery under general anesthesia via endotracheal intubation with propofol were consented for the study.

4.4.2. Exclusion criteria

- Patient is on opioid analgesic.
- Phenothiazine, tranquilizer.
- Sedatives, hypnotics or any other CNS depressant before anesthesia like diazepam
- History of using sedatives, hypnotic's medication.
- All Pregnant mothers.
- Lactating women as well as patients.
- With a history of allergy to propofol.
- Patients who refused.
- Hypotensive or hypertensive patients and.
- Patients with cardiovascular or respiratory disease.

- Patients with alular heart disease.
- Psychiatric patients.
- Patient on medication like beta blocker.
- Baseline heart rate more than 120 beat /minute.

4.5. Study variable

4.5.1. Dependent variables

- Mean induction dose of propofol.
- Hemodynamic parameter.
- Propofol injection pain during induction.

4.5.2. Independent variables

- Age, sex, weight, height, BMI,ASA status
- Priming dose of Propofol

4.5.3. Controlled variables

- Propofol dose/kg
- Premedication given
- Concentration of Propofol
- Speed of injection
- Type of propofol
- Type of Vein used
- Duration of priming

4.6. OPERATIONAL DEFINITION

Baseline vital sign- vital sign before of induction of Anesthesia.

ASA status: is a surgical risk stratifications validated by American Society of Anesthesiologist [50].

Described as follows:

ASA I: the healthy individual having no organic, physiological, or mental disorders

ASA II: managed medical diseases without functional limitations and only mild systemic impacts.

ASA III: health illness with serious systemic effects and functional limitations.

ASA IV: Uncontrolled medical disorders can pose a hazard to life due to the severe functional ability deterioration they are connected with.

Elective Surgery: Non-emergent surgical cases that were assigned to surgery were among the scheduled operations.

Propofol Injection pain: It is pain brought on by the IV injection of propofol.

Numeric pain rating scale: An 11-point size, the NPRS has a rating between 0 and 10 [51].

Priming principle: also known as auto co-induction has been used to describe the practice of administering a 25% pre-calculated dose of induction agent prior to giving the full dose of the same agent [27].

The spectral index (BIS) is a monitoring modality that uses a processed electroencephalogram signal to quantify the depth of anesthesia or sedation.

4.7. SAMPLE SIZE DETERMINATION AND SAMPLING TECHNIQUE

4.7.1. Sample size

We utilized the formula for sample size calculation with continuous results for two independent samples. Based on the findings of a new research conducted in Nigeria, the prime group received a considerably lower mean induction dose of propofol (120.27 ±16.20) than the control group (133.58 ±24.25) (P = 0.0006). With $\mu 1 = 120.27$, $\sigma 1 = 16.20$ and $\mu 2 = 133.58$, $\sigma 2 = 24.25$ with an alpha error of 0.05 at a power of 80% [37].

$n = \sigma 1 * \sigma 1 + \sigma 2 * \sigma 2 * (Z1 + Z\,2 * Z1 + Z\,2) / \mu 2 - \mu 1$

16.20 *16.20 +24.25 *24.25 *(1.96+0.84 *1.96+0.84)/ 133.58-120.n =39.455=40

Both groups n= 40x 2 = 80 and adding 10%.

Then total sample size is N=88.

n=88

4.7.2. SAMPLING TECHNIQUE

ADDIS ABABA SELECTED PUBLIC HOSPITALS

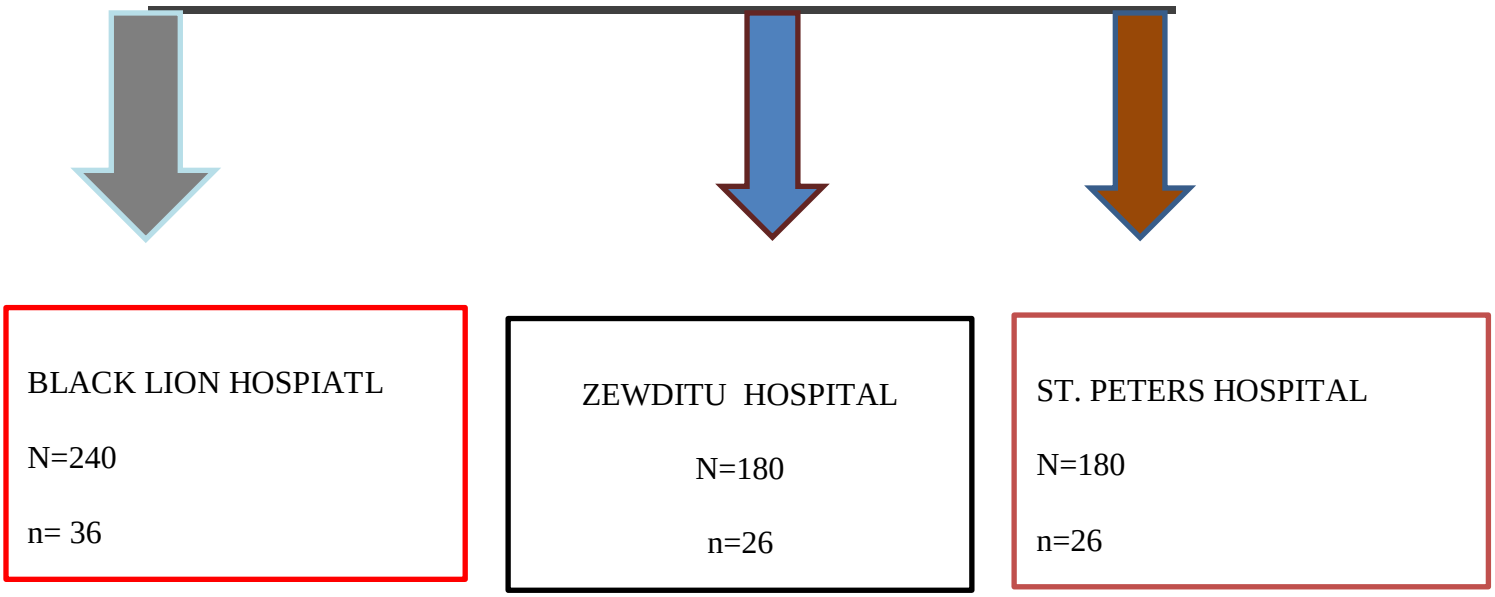


Figure 3; Proportional allocations for sample size

For a month, an assessment of the situation was conducted. on average 3 patient daily or 60 patients monthly were undergone operation with propofol in Zewditu memorial hospital.

- The equation K=N/n, whereby n is the total number of samples taken and N is the population done within 3 months was used to find the sampling interval K.
  K= 180/26 ≈ 6
- Consequently, the sampling window became Six and the first person selected by lottery method from daily operation.

Selected using lottery method from those fulfills criteria. The sampling frame for the first case selected by lottery method is daily operation list among patient induced with propofol in Zewditu memorial hospital.

- Then, every 6cases who induced study drugs were Included in study groups until the required sample size was filled during the study period.

Similar to Zewditu memorial hospital for a month, an assessment of the situation was conducted. on average 3 patient daily or 60 patients monthly were undergone operation with propofol in in peteres hospital.

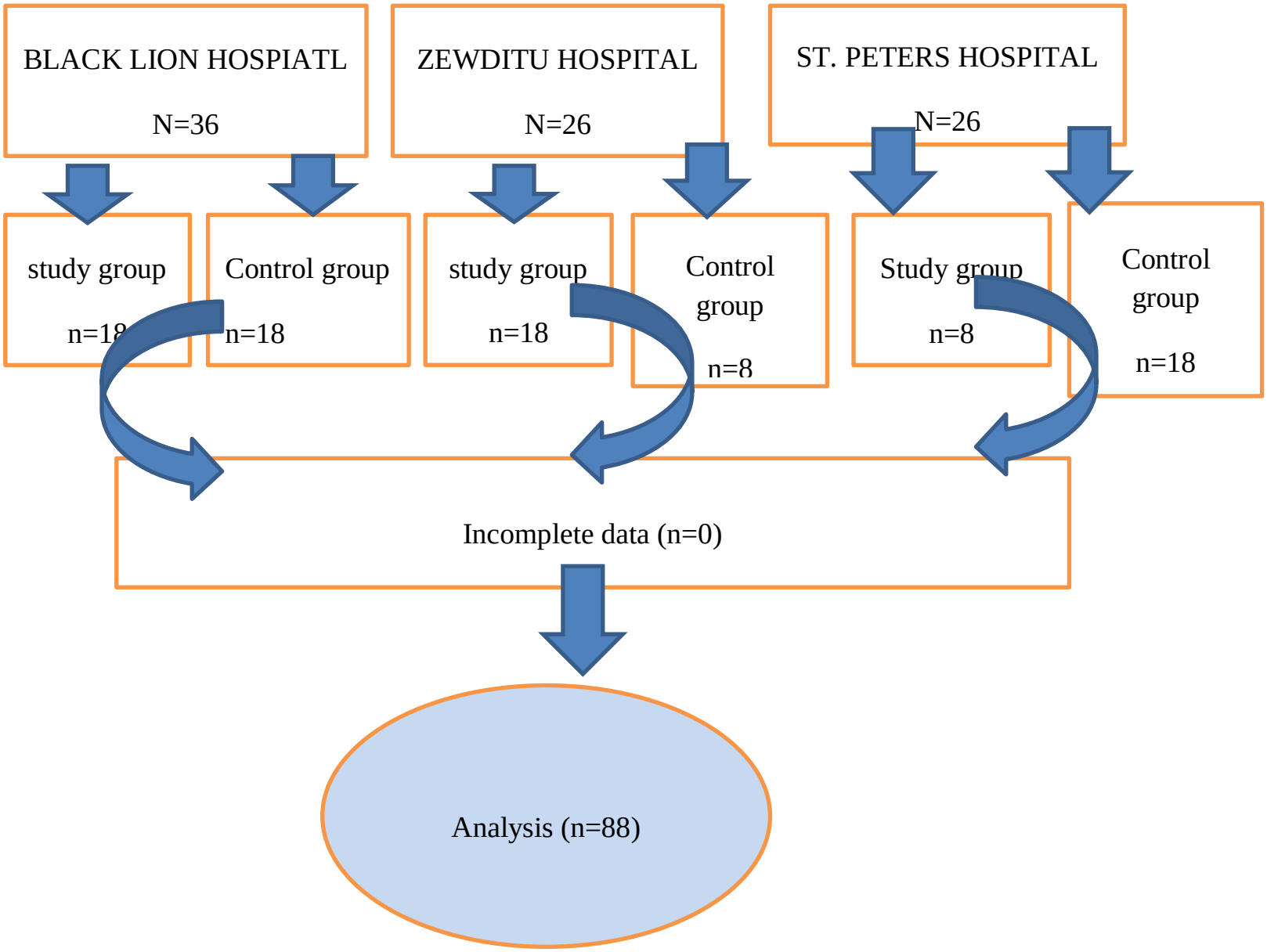
- The equation K=N/n, whereby n is the total number of samples taken and N is the population done within 3 months was used to find the sampling interval K.
  K= 180/26 ≈ 6.
- Consequently, the sampling window became Six and the first person selected by lottery method from daily operation.

The sampling frame for the first case selected by lottery method is daily operation list among patient induced with propofol in petered hospital.

- Then, every 6cases who induced study drugs were Included in study groups until the required sample size was filled during the study period.
  For a month, an assessment of the situation was conducted. On average 4 patient daily or 80 patients monthly were undergone operation with propofol in Tikur Anbessa Specialized Hospital.
- The equation K=N/n, whereby n is the total number of samples taken and N is the population done within 3 months was used to find the sampling interval K.
  K= 240/36 ≈ 6.
- Consequently, the sampling window became Six and the first person selected by lottery method from daily operation.

The sampling frame for the first case selected by lottery method is daily operation list among patient induced with propofol in Tikur Anbessa Specialized Hospital. Then, every 6cases who induced study drugs were Included in study groups until the required sample size was filled during the study period.

Figure 4: enrolment of Electives Surgeries under General Anesthesia in selected Public Hospital Addis Ababa Ethiopia from February 1 To April 30, 2022/2023.



4.7.3. Data collection instruments, procedure and patient handling

Semi-structure interviewer-administered questionnaires and operation room monitor were used to collect the data. The tools of data collection were being pre-tested. This helped in making

appropriate corrections where necessary. Four anesthetists were being trained as research assistants for a day by the principal researcher to provide aid with the administration of the questionnaire. The patient was being given a detailed explanation of the research in a language they can understand, and a signed informed consent was then obtained. The day before surgery, the patient were have a preoperative visit on the ward, during which their weight, blood pressure, respiration rate, and other pertinent clinical indicators were be noted. All patients were brought to the operating room in the morning of the procedure, and a cannula was placed on the dorsum of the hand to secure an intravenous access. Then our patient was preoxgenated.then Group I received 0.6 mg/kg IV of propofol (25%, of the pre-calculated induction dose) while group II induced with routine technique. 30, second later, all two groups received IV induction 2.5mg/kg propofol until loss of verbal response and eye lash reflex was attained. Propofol mg/kg, priming propofol dose mg/kg, total dose administered, duration of priming which is 30 second was recorded. BP ,DBP, MAP and HR were recorded at baseline(just before induction), 1 minute after induction ,immediately ,5, 10, minutes after intubation intraoperative in both group I and groupII. We rate the severity of the pain during intravenous induction using the numeric evaluation scale.

4.7.4. Data control

1. Before beginning the real gathering of data, the checklist of questions had been evaluated on a few samples at Zewditu Memorial and St. Peter's Hospital.
2. Data collectors included anesthesia professionals with experience in gathering intraoperative information.
3. Data collectors received orientation and training that included the purpose and method of data collection.
4. A close follow up was kept on the information collection process.
5. Every questionnaire was reviewed by the coordinator each day, and communicated their findings to the Principle Investigator that same day.
6. The lead investigator verified the collected data every day.

4.7.5. Data analysis.

SPSS version 26 software was being used to analyses and evaluate the collected data. In frequencies and percentages, qualitative information like sex and marital status was being displayed. When applicable, the mean and standard deviation was be utilized for quantitative data. Shapiro wilk test and histogram was performed to determine whether the outcome dispersion were regular, followed by independent t-tests for normative data, Mann-Whitney U-tests for nonparametric data, and chi-square tests for categorical data. The level of statistical significance for all tests taken AS $P < 0.05$**.**We used Levine's test to assess homogeneity of variance which equal variance was assumed with p value >0.05.

5. ETHICAL CONSEDERATION

Ethical clearance was obtained from the department ethical clearance committee before the start of the study. Then Support letters was being sent to each hospital, and authorization for data collection was being requested from the hospital administration. Before administering anesthesia, each subject was having their verbal informed consent obtained after being informed of the study's goals and significance. Using an anonymous questionnaire allowed for the maintenance of confidentiality throughout the entire investigation.

6. RESULT DISSMINATION

Copies of the final results will be given to each hospital, the Ethiopian Association of Anesthetists, TASH, and the AU. The study's findings could possibly be published in an international journal.

CHAPTER FIVE: RESULT AND DISCUSSION

5. RESULTS

5.1 demographic and clinical characteristics of the patient

In this study, a total of 88 patients were included. 44 among the 88 patient were in the priming group, one who takes 0.6mg/kg or25% of the induction dose propofol and 44 where non –exposed group who take nothing. Age, weight, ASA status, and sex between the two groups did not significantly differ. independent samples t test and chi square test where done and Among groups, there was comparability in the demographic condition (table 1).

Table1**:** sociodemographics characteristic patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023(n=44).

Demographic data	Exposed- group=44 Means	Non -exposed group n=44 mean±SD	P-value
Age(year)	43.16 ±14.595	43.77±2.91	0.79
Sex male/female	24(54.5%0/20(44.5%)	17(38.6%)/27(61.4%)	1.35
ASA I/II (n/%)	25(56.8%)/19(43.2%)	21(47.7%)/23(52.3%)	0.393
Weight(kg)	63.86±7.911	61.95±7.424	2.46
Mean height (m)	1.68±0.65	1.62±0.454	2.74
BMI**	22.9184±1.293	23.0371±2.214	0.789

SD standard deviation. : Independent samples t test: $\chi 2$chi square test

5.2 Comparing mean induction dose of propofol between exposed and non -exposed group

In this research, there was a statistically significant decrease in the average induction the dosage of propofol after priming, with the mean induction dose in exposed group (group I) being 142.64±14.591 as opposed to 154±10.296 in non -exposed group (group II)($p = 0.001$), indicating a 8% reduction.

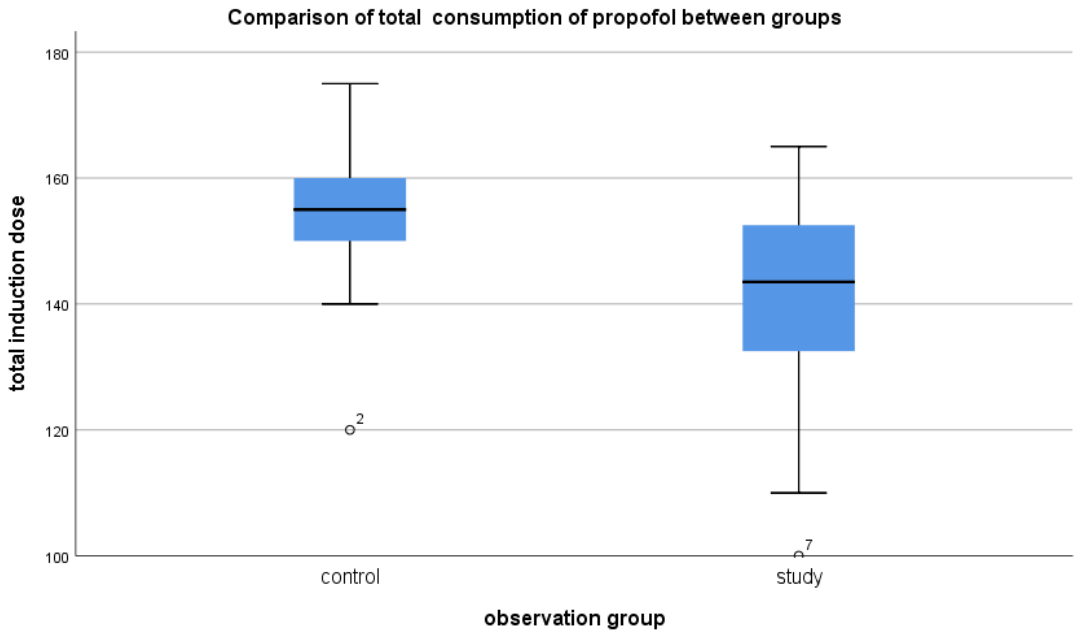


Figure 5

figure 5: comparison of mean induction dose of propofol (mg/kg) b/n exposed and non-exposed control group in in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.

Mean +SD (standard deviation): independent samples t test was used

5.2 Comparing hemodynamic parameter between Exposed and Non -exposed group

Immediately after 1 minute if induction the heart rate91.55in Non -exposed and75.20 in Exposed- group with p- value {0.000] this show that there is significant heart rate incensement in none- exposed group than exposed study group.

Mean heart rate	Exposed- group (n=44) mean±sd, M =median	Non -exposed (n=44) group mean±sd, M =median	p-value
Before induction	72. ±.8251	75.14 +7.911	0.126
1minute After Induction	75.00	92.50	0.000
Immediately after intubation	75.70±9.802	81.34+8.983	0.006
5 minute Min After induction	76.25±9.512	84.11+9.117	0.000
10 minute Min After induction	73..95±8.449	77.95+11.27	0.630

Table 2: comparison of mean heart rate between Exposed- group study and Non -exposed group in in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.mean SD.

SD: standard deviation; independent samples t test: mann_whitney test

Look at next three tables they show that blood pressure parameter were, significantly different.

Systolic blood pressure	Exposed- group (n=44) mean±sd M =median	Exposed- group (n=44) mean±sd M =median	p-value
Before induction	125.000	120.000	0.252
1minute After Induction	117.522±15.25	109.159±10. 6	0.001
Immediately after intubation	121.11±13.04	128±13.35	0.0011
5 minute After induction	116±7.212	105.88±9.18	0.000
10 minute After induction	112.13±15.28	107.22±11. 06	0.88

Table3: comparison of mean systolic blood pressure between Exposed- group and Non -exposed group in in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023. MEAN ±SD.

SD: standard deviation. : Independent samples t test mann_whitney test*

Table2: comparison of mean diastolic pressure between Exposed- group and Non –exposed in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.mean±sd, M =median

diastolic blood pressure	Exposed- group (n=44) group mean±sd M =median	Non -exposed (n=44) group mean±sd M =median	p-value
Before induction	76.00	70.000	.185
1minute After induction	74.25±9.01	66.93±12.44	0.000
Immediately after intubation	75.500	87.500	0.000
5 minute After induction	67.250	66.500	0.003
10 minute After induction	67.500	66.500	0.006

SD: standard Deviation. Independent samples t test; mann_whitney

Table3: comparison of mean blood pressure between Exposed- group and Non –exposed group in in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.Mean±SD.

Meanbloodpressure	Exposed- group (n=44) group mean±sd	Non -exposed (n=44) group mean±sd	p-value
Before induction	91.15±8.54	89.1±8.62	0.278
1minute After induction	86.2±8,99	79.77±77	0.001
Immediately after intubation	91.81±9.08	100.45±9.08	0.000
5 minute After induction	89.68±8.30	80.94±6.49	0.000
10 minute After induction	87.00±9. 44	81.31±9.52	0.006

SD: standard deviation; independent samples t test

5.3 Comparing overall incidence and severity of propofol injection pain between two groups

Overall incidence of pain is 90.9% in Non -exposed group and 63.6% in r exposed group with (p=0.002).

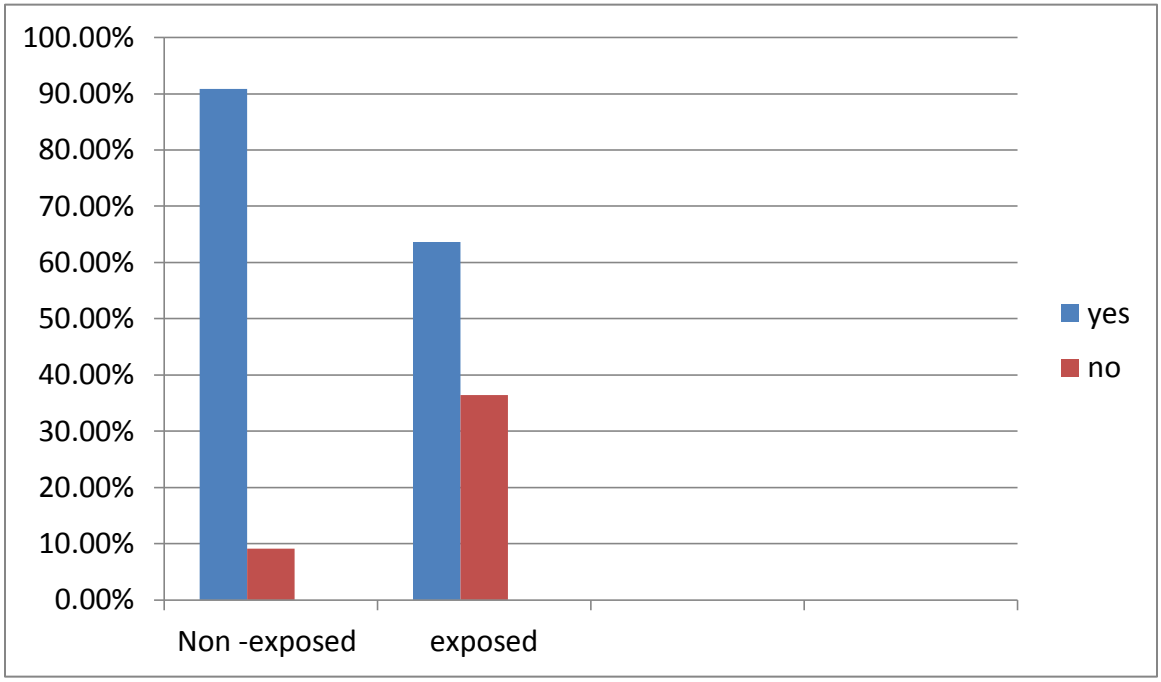


Figure6: comparison incidence of pain on injection of propofol between Exposed- group and non- exposed group in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.X 2 =chi-square used.

The main dose of propofol produced a maximum level (grade3 or severe) of local pain on 18 patient among 44 in non-exposed group, which is high 4 in exposed group among 44.

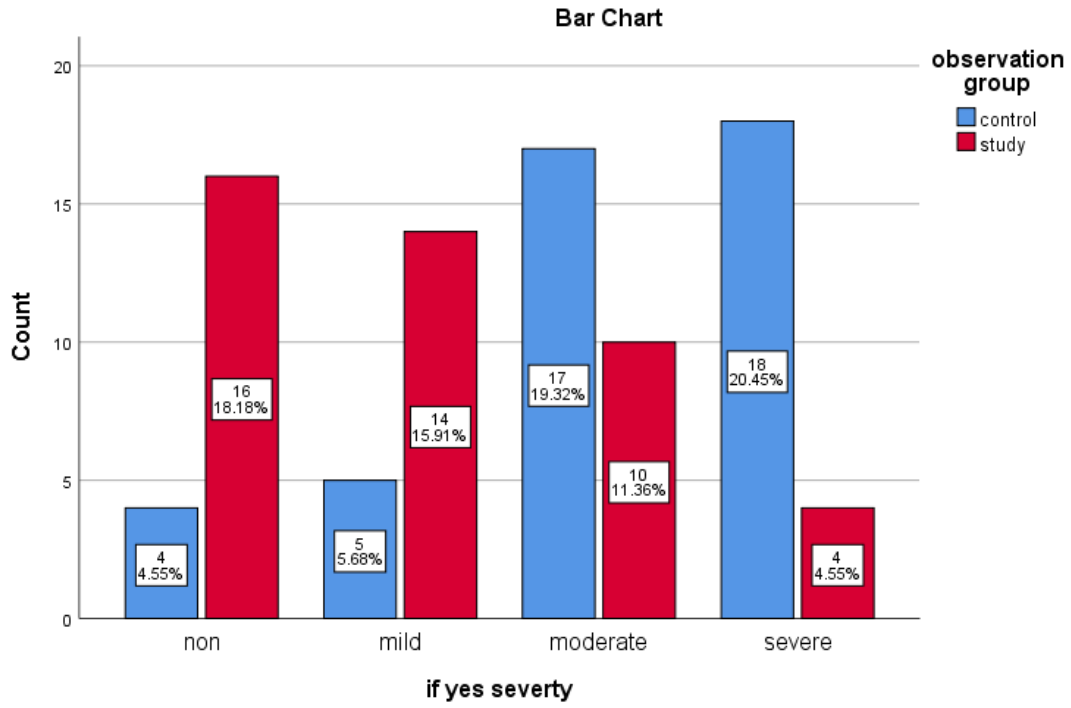


figure7: comparison on PAIN LEVEL of propofol between study and control group in in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023..X 2 =chi-square used.

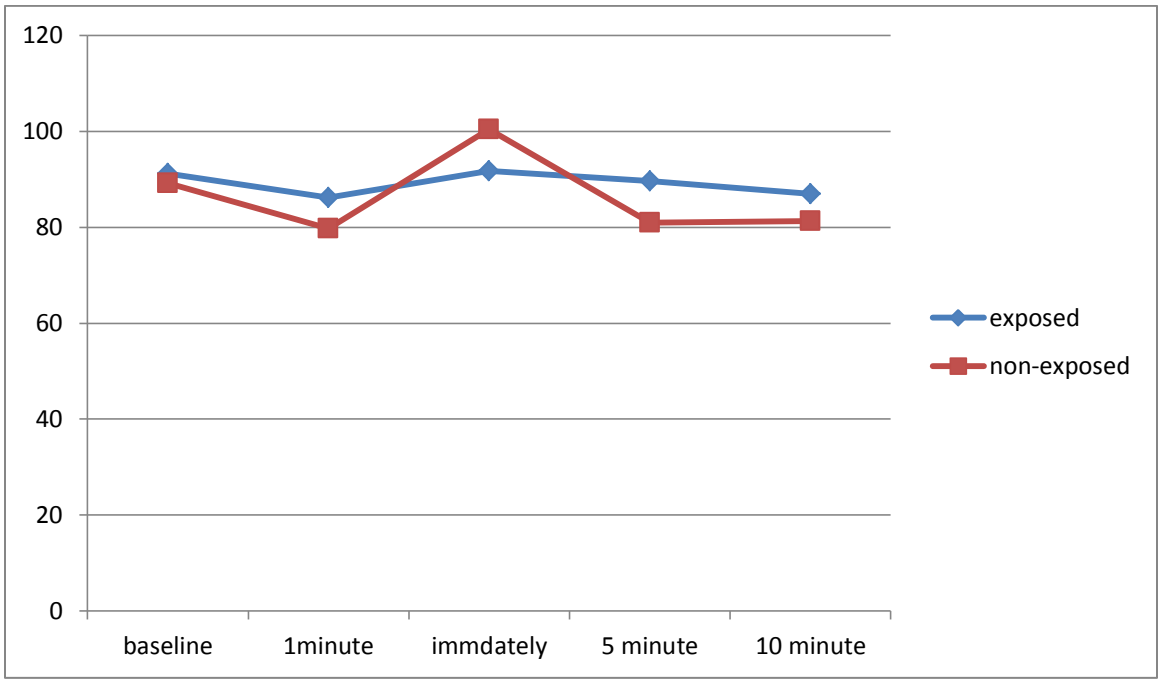


Figure 8: Trend mean blood pressure in Exposed- group and non-Exposed group in patient undergoing electives surgeries under general anesthesia selected public hospital Addis Ababa Ethiopia from February 1 to April 30, 2022/2023.

5.2 DISCUSSION

The priming concept to reduce propofol could be a more effective approach with fewer negative consequences. As a result, we carried out observational study using the priming concept for the induction dose of propofol and evaluated the overall dosage requirement as well as the associated hemodynamic alterations. We applied 25% (0.6 mg/kg) of the calculated dose as the propofol priming dose, with a standard propofol dose of 2.5 mg/kg.

In this research, there was a statistically significant decrease in the average induction the dosage of propofol after priming, with the mean induction dose in exposed group (group I) being142.64±14.591 as opposed to 154±10.296 in non- exposed group (group II)($p = 0.001$), indicating a 8% reduction in induction dose of propofol. We observed a highly significant reduction in our study. The decrease in induction dosage noticed by using the 'Priming Principle' may have been explainfol anxiolytic impact at sub hypnotic doses (38).

Investigations conducted by Anil et al., Anderson and Robb, Srivastava et al., and Djaiani and Ribes similarly demonstrated a reduction in induction dosage need following priming, to variable degrees [15, .36,46].

In line to this study research done by (Tanga} show mean reduction of propofol by 27%, in group I (the control), the mean induction dose of propofol is 135.3 mg, while in group II (the test), it is 92.7 mg (p-value 0.01) [39]. As a result, Group II dose requirements are significantly lower than those of Group I. This show large amount reduction when we compare from this study this may be as result of Fentanyl premedication (1 microgram per kilogram) given over 30 seconds in their study. Propofol dosage necessary for unconsciousness and demonstrated that it is decreased by raising the fentanyl dosage [22]. The other reason may be(Midazolam 0.02 mg. per kg) their study It is known that pretreatment with midazolam lowers the induction dose needed for propofol.

Congruent with this study similar large mean induction dosage reduction found in study done by {Monga,}. Showed that in study group, the mean induction dose was 81.229.68, while in the control group, it was 113.0212.63 with p value of {0.001} [27]. (Glycopyrolate 0.004mg/kg) IV ,(Midazolam 0.03 mg/kg) IV 15 minutes before induction and Fentanyl 1µg/kg over 30minute

were premeditated in their study.so this premedication can have significant effect for this large amount of mean induction dose decreasement .

Another study by {Priya,} in study group, the mean induction dose was 80.37 14.82, while in control group, it was 112.27 17.68. Thus, we saw that group Sor study group required a 30% lower induction dose [43].

Another study conducted by {Srivastava,} shows the maximum reduction which is 40%. Srivastava premeditated his patient with fentanyl 1 µg/kg 20 mg of lignocaine .the duration of priming is 2 minute [44]. When we compare from this study the mean induction dose significantly decreased in Srivastava this may be fentanyl premedication in and long priming duration which is 2 minute in Srivastava but 30 second in my study.

In line to this study, study done by {Kataria, etal} show that In comparison to the control group, the mean inducing dosage need was determined to be 31.88% lower in the propofol auto-co-induction group with P<0.001) [25].

Immediately after 1 minute of induction the heart rate91.55in none- exposed and75.20 in exposed group with p- value {0.000] this show that there is significant heart rate increasment in none- exposed group than exposed group.

In line with this result study done by{Biswal, 2018 #12} indicate The HR proved statistically significant (p = 0.003) at one minute following induction, measuring 80.19.78 beats per minute in none- exposed and 74.628.2 beats per minute in exposed [22].

Immediately after intubation there was increase in heart rate in exposed priming group and in none- exposed group in our study. This observation was different from the result observed in Biswal work. The mean HR was not changed statistically between 5 minutes after induction and right away after intubation in Biswal work [26] .such kind of heart rate phenomena was also observed in different work like Maroof et al, A. Kumar et al and Fairfield et a [2] .this was contrary to this study. This may be due to administration of midazolam as a pre-medic ant five minutes before induction (0.03 mL kg-1) by Basal and the application of Promethazine 0.025 mL kg-1 and Meperidine 1mL/ kg1 by Maroof et al.

The maximum increase in heart rate in this study is immediately1 minute after induction in non-exposed group from 75 to 91beat/minute (value=0.000). The next maximum increase in heart

rate is 5 minute after induction from 75 to 84 beat/minute in none- exposed group with p-value =0.000. The minimum increase in heart rate is 10 minute after induction from 75 to 77beat /minute and immediately after intubation from 75 to81 beat /minute. From this we can observe that, on the cardiovascular system, propofol is known to have a biphasic action. First, the first few minutes following injection are characterized by a drop in mean arterial pressure and systemic vascular resistance. This drop in mean arterial pressure and systemic vascular resistance generates a surge in the sympathetic nervous system, which is controlled by the carotid sinus and aortic arch baroreceptors and results in an increase in heart rate. Second, the heart rate and stroke volume begin to decline to their initial values 2 minutes after injection, despite systemic vascular resistance that is lower than normal. Propofol is blamed for "resetting" the baroreceptor reflex to a lower pressure value than usual due to propofol [27].

In line with this study, research done by (Biswal P) the systolic blood pressure was significantly lower in control group decreased by 11.82% at one minute after induction, immediately after intubation by11.36% and 5 minutes after inductionby 6.91% than in study group. Similarly the diastolic blood pressure and mean arterial pressure values were significantly lower in control group at one minute after induction by 5.35%, 8.2% respectively, immediately after intubation by 3.99%, 7.23%respectevely and 5 minutes after induction by 2.2%, 4.27% respectively than in study group [26].

congruent with this study in research done by(Anil K) there was a lesser fall in MAP at one minute after induction(99.16±12.160,during intubation(83.03±11.9),immediately after intubation(82.66±11.5) and 5 minutes later(85.23±11.9) in control group whereas in study group MAP one minute after induction(94.6±10.2) during intubation(96.86±8.46) ,immediately after intubation (98.8±9.15), and 5 minutes late (95.23±9.77) [15].

This study shows that the incidence of pain in none- exposed group is 40(90.9%) whereas in exposed group is 28 (63.6%). In line to this study done by {Biswal,} the overall incidence of pain is 95% in control group and 81.7% in primed or study group [26].

CHAPTER SIX - STRENGETH AND LIMITATION

6.1 strength of the study

- The strength of these study participants was homogeneous between the two groups.
- The two groups were comparable in socio demographic distribution.

6.2limitation of the study.

- Lack of randomization and control

CHAPTER SEVEN; CONCLUSION AND RECOMMENDATION

7.1. Conclusion

An application of 25% (0,6mg/kg) of the induction dose of propofol associated mean reduction propofol dose by 8 %and improved hemodynamic stability. Propofol priming also associated with a considerably decreased incidence of pain.

7.2. RECOMMENDATION

For anesthetists

- ❖ Anesthetist should use priming principle
- ❖ Anesthesia professional should get training on priming principle

For further researchers

- ❖ Further study should be done on this area

- ✓ Effect of priming principle on propofol injection pain
- ✓ Optimal priming dose of propofol should be studied
- ✓ Effect of priming principle on suxamethionum fasculation
- ✓ Effect of priming principle by using bi spectral index

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9. ANNEXES

Annex one consent form

አድስ አበባ ዩኒቨርሲቲ ጤና ሳይንስ ኮሌጅ፣ ህክምና ትምህርት ቤት፣የአንስቴዥያ ትምህርት ክፍ

የመጠይቅ ፈቃደኛነት ቅጽ

ስሜ _____ ይባላል፡፡ እኔ በአዲስ አበባ ዩኒቨርሲቲ በአንስቴዝያ ትምህርት ክፍል የምርምር ቡድን ዉስጥ አንድ አባል ነኝ፡፡የዚህ መጠይቅ አላማ ከኦፐራሲዎንበፊት የአንስቴዥያ መድሃኒት ፕሮፖፎል መጠን ለመቀነስ ሲሆን ተከትሎ ስለሚከሰተዉ የደም ግፊት መቀነስ እና ህመም ለመቀነስ ምርምር/ጥናት /መረጃ ለመሰብሰብ ነው፡፡ እርስዎን አንድ የጥናቱ ክፍል አድርጌ ስመርጠዎ አስፈላጊ የሆኑ መረጃዎችን እንደሚሰጡኝ በማሰብ ነዉ፡፡በጥናቱ ለመሳተፍ ፈቃደኛ ከሆኑ ከእርስዎ የሚገኘው ማንኛውም መረጃ በሚስጥር ይጠበቃል፡፡ለዚህም ሲባል የእርስዎ ሥምም ሆነ አድራሻ አይገለጽም፡፡፡እንድሁም ከጥናቱ በኋላ ኦፐራሲዎን ለሚደረግላቸዉ ታካሚዎች ፣የፕሮፖፎል መጠን በመቀነስ ተከትሎ የሚከሰተዉን የደም ግፊት መቀነስ እና ህመም መቀነስ ይቻላል።

የቃል ሥምምነት

የዚህ ጥናት ዓላማው ገብቶኝ በጥናቱ ለመሣተፍ

ሀ. ፈቃደኛ ሆኛለሁ ለ. ፈቃደኛ አይደለሁም

በጥናቱ ለመሳተፍ ፈቃደኛ ከሆኑ ቃለመጠይቁን መቀጠል ይቻላል፡፡

ፈቃደኛ ከሆኑ የመጠይቁ መለያ ቁጥር_____መጠይቁ የተካሄደበት ቀን _____

የጠያቂው ሥምና ፊርማ _____

የሱፐርቫይዘር ስምና ፊርማ _____

ጥናቱን በተመለከተ ማንኛዉም አይነት ጥያቄ ካላችሁ የሚከተለዉን አድራሻ ተጠቀሙ

Annex: II Information sheet

Hello.

My name is _____. I

I am a researcher who has been enrolled in Addis Ababa University's postgraduate program in anesthesia. I'm going to study Effect Of Priming Principle on the Iduction Dose Reqireement Of Propofol And. Its Effect on Hemodynamic Parameter and Pain At Injection Site in Patient Undergoing Electives Surgeries Under General Anesthesia Public Hospital Addis Ababa Ethiopia From February 1 To April 30, 2022/2023.Your involvement is crucial to the accomplishment of this investigation, but please be aware that everything we gather here is for research reasons only, and that the data will not be used by anyone other than this research, so privacy can be ensured. your names will be kept anonymous. the data collected will help the government and other accountable organizations achieve a reduction in morbid complications after operation and patient satisfaction.

Do you want to continue yes---------- No---------- (Thank you in advance for your help!)

Name and contact address of investigators

gebrehana gebre +251 0996864354

Fast198826@gmail.com

Annex: two data collection instrument

SECTION 1; SOCIODEMOGRAPHIC DATA (CHART REVIEW)

socio demographic and preoperative clinical characteristics of elective surgical patients who underwent elective surgery at tash,zewidtu memorial hospital,st,petres hospital, from February to April 30/2015 each.

SECTION I: SOCIODEMOGRAPHIC DATA (CHART REVIEW)

Bed no:	Card number:		Code
S.no	Question	Response	
1.1	Age		
1,2	ASA STATUS (I, II,I)	A. ASA I B. ASA II	
1.3	Sex	A. Male B. Female	
1.4	Weight		
1.5	Height		
1.6	BMI		

Section II: Data during the preoperative period

No	Question	response	
2.1	base line data before the operation 1.heart rate, 2.sbp 3dbp 4,map	1…….bpm 2…….mmhg 3…….mmhg 4…….mmhg	
2.2	Diagnosis	……..	
2.3	does the patient takepremedicattion orally or Ivor intramuscularly within 30minute –3hr before surgery?	1. yes 2, no	if no skip no 2.4
2.4	if yes, specify the drug, and duration of time from administration to skin incision?	……./……. ……..	
2.5	does the patient take preemptive analgesia	1. yes 2, no	if no skip no 2.6

	medications orally or intramuscularly within 1 –3hr before surgery?		
2.6	if yes, specify the drug, and duration of time from administration to skin incision?	……/……. ……..	

questions related to anesthetic and surgical intervention surgical patients who underwent elective surgery at tash, zewidtu memorial hospital, st, petres hospital, from February 1 to April 30/2015

SECTION III: QUESTIONS RELATED TO ANESTHETIC AND SURGICAL INTERVENTION

3.0. propofol dose calculated mg/ kg……..

3.1. prming dose or 25% of the induction dose in study group…….

3.1. total dose of propofol required to induce patient in study group (priming dose +next induction dose) (mg)……

3.3 . . . . total dose of propofol required to induce patient in control group (mg)…….

3.4 .does additional propofol added? if yes how much (mg)…….

3.2 HEMODYNAMIC PARAMETERS

	heart rate (bum	systolic bp (mmhg)	diastolic bp (mmhg)	mean bp (mmgh
before induction				
1 min after induction				
immediately after intubation				
5 min after intubation				
10. min after intubation				

3.3: QUESTION ABOUT PROPOFOL INJECTION PAIN

1. what is the type of propofol used?

along chain .b medium chain c.combnation of the two

2. what is the type of propofol?

aliped based b.non lipid based c.prodrug

3 what are the concentration of propofol…….

4. what is the type of vein used?

a.larg vein small vein

5. what is speed of injection?

a.4omg/10sec b.or</> 40mg/10sec

6. occlusion of vein while injection

a.yes b .no

7. are their comp nation of drug with propofol?

a.yes b.no

8 if no/7 are yes what are the drug……

1. did the patient feel pain during injection of propofol?

a. yes

b. no

2. If yes, what is severity of this pain as measured by numeric rating scale (VRS) during injection of Propofol?

APPENDIX I ENGLISH VERSION OF NUMERIC RATING SCALE (NRS)

The scale was used to assess propofol injection pain patient was asked to rate their pain was assessed and recorded at induction of anesthesia with propofol in both group.

The patient was asked one of the following questions:

A. What number on a 0 to 10 scale would you give your pain right now?

B. When the explanation suggested above is not sufficient for the patient, further explanation or conceptualization of the scale will be done:

0 = no pain

1-3 = mild pain (nagging, annoying, interfering little with ADLS)

4–6 = moderate pain (interferes significantly with ADLS)

7-10= severe pain (disabling; unable to perform ADLs)

APPENDIX II አማርኛ ትርጉም በቁጥርአምሳያመለኪያ (NRS)

በዚህ መለኪያ በሽተኛዉየሚጠየቃቸዉጥያቄዎችአሁንየሚሰማዎትንህመምበየትኛዉቁጥርይወክሉታል;

ሀ) ከዜሮእስከአስርካሉትቁጥሮችአሁንየሚሰማዎትንህመምየትኛዉቁጥርይገልፀዋል.

ለ) ከላይየተሰጠዉማብራሪያበቂሳይሆንሲቀር፣ለበሽተኛዉየበለጠመረጃመስጠትአስፈላጊሆኖይገኛል

0- ምንምህመምየለም

1-3 - ትንሽህመምአለ

4-6 - መካከለኛህመምአለ

7-10 - ከባድህመምአለ

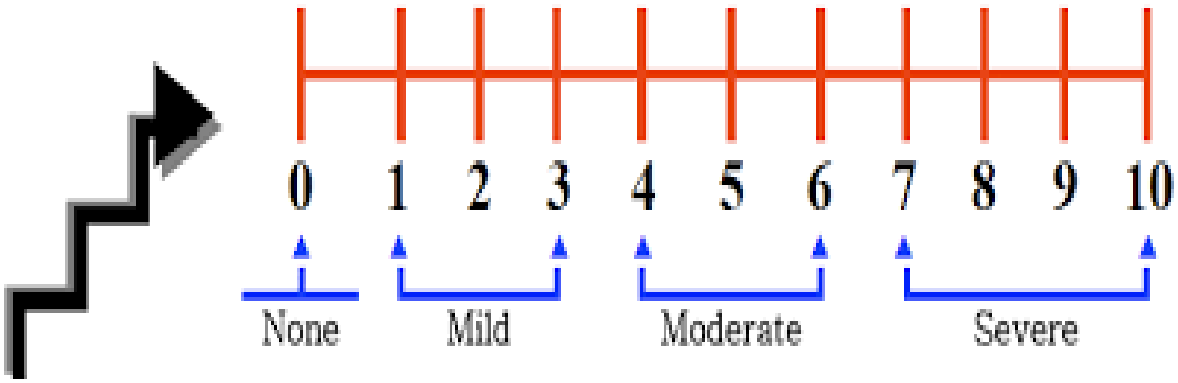

FIGURE 9;ADOPTED NUMERIC RETING SCALE PAIN ASSIMENT GUIDELINE